

The Mouse Genome Database genotypes::phenotypes

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ABSTRACT

The Mouse Genome Database (MGD, <http://www.informatics.jax.org/>), integrates genetic, genomic and phenotypic information about the laboratory mouse, a primary animal model for studying human biology and disease. Information in MGD is obtained from diverse sources, including the scientific literature and external databases, such as EntrezGene, UniProt and GenBank. In addition to its extensive collection of phenotypic allele information for mouse genes that is curated from the published biomedical literature and researcher submission, MGI includes a comprehensive representation of mouse genes including sequence, functional (GO) and comparative information. MGD provides a data mining platform that enables the development of translational research hypotheses based on comparative genotype, phenotype and functional analyses. MGI can be accessed by a variety of methods including web-based search forms, a genome sequence browser and downloadable database reports. Programmatic access is available using web services. Recent improvements in MGD described here include the unified mouse gene catalog for NCBI Build 37 of the reference genome assembly, and improved representation of mouse mutants and phenotypes.

INTRODUCTION

The Mouse Genome Database (MGD) is a comprehensive public resource providing integrated access to genetics,

genomics, functional and phenotypic data for the laboratory mouse (1–3). MGD is a core database component of the Mouse Genome Informatics (MGI) database resource (<http://www.informatics.jax.org/>). Other resources that are integrated with MGD as part of the MGI resource include the Gene Expression Database (GXD) (4), the Mouse Tumor Biology Database (MTB) (5) and the Gene Ontology (GO) project (6).

MGD facilitates translational biomedical research via a comprehensive database resource integrated with bio-ontological semantic standards that enhances the use of the laboratory mouse as a model animal system for studying human biology. Primary data types in MGD include sequences, genetic and physical maps, genes, gene function, gene families, strains, mutant phenotypes, SNPs, animal models of human disease and mammalian homology. MGD annotations are integrated through a combination of expert human curation and automated processes. Examples of vocabularies and ontologies utilized in MGD include the GO (6), Mammalian Phenotype (MP) Ontology (7) and the Anatomical Dictionary of Mouse Development (8). Mouse genes and gene products in MGD are also associated with multiple other informatics resources including the Online Mendelian Inheritance in Man (OMIM), UniProt protein resources and PIR protein super family classifications. MGI is the authoritative source for mouse gene and strain nomenclature and GO functional annotations. MGI is the most comprehensive public resource of information on mouse phenotypes and associations between mouse models and human disease.

Data in MGD are updated daily. Data access is accomplished via dynamically generated web pages, text files available via FTP (updated nightly) and through direct SQL (account is required). In general, there are 4–6 major software releases per year to support access and

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Table 1. Snapshot of data content in MGD: 26 September 2008

MGD data statistics	26 September 2008
Genes with nucleotide sequence data	28 869
Genes with protein sequence data	27 244
Genes (including uncloned mutations)	37 696
Genes with gene traps	12 390
Mapped genes and markers	46 288
Genes with GO annotations	18 082
Mouse/human orthologs	16 685
Mouse/rat orthologs	15 787
Phenotypic alleles	20 478
Genes with one or more phenotypic alleles	7 876
Phenotypic alleles that are targeted mutations	12 338
Genes with targeted mutations	5 306
Human diseases with one or more mouse models	858
QTLs	3 979
References	133 867
Mouse RefSNPs	10 089 692
Mouse nucleotide sequences integrated into the MGI system (includes ESTs)	>8 750 000

Only genes with nucleotide sequence data are included in the unified gene catalog.

display of new data types. A recent summary of MGD content is shown in Table 1.

2008 IMPROVEMENTS AND UPDATES

New ways to explore mouse phenotypes

The Allele Detail page for each mutant allele in MGI now includes two distinct views of phenotype data that provide powerful options for exploring relationships between genotypes and phenotypes (Figure 1).

In the 'Phenotype summary' section of the page, a matrix view of phenotypes (vertical axis) by genotypes (horizontal axis) allows users to quickly view the range of phenotypic effects observed for a given allele. The effects of different allelic combinations (such as homozygous, heterozygous, conditional and complex) in different genetic backgrounds can be compared. The general phenotype classes can be expanded individually (as shown in Figure 2A) or all phenotype terms can be viewed or hidden using the 'show'/'hide' option in the matrix header. This matrix view can also be used to go directly to the phenotypic details for a specific genotype (displayed in a new window) by clicking on its genotype abbreviation (e.g. hm1, for homozygous 1).

The 'Phenotypic data by genotype' section presents a table of all genotypes involving the allele being viewed. Each genotype is a link that expands to reveal the full phenotype details for that genotype, including disease model associations (Figure 2B). Details for all genotypes containing the mutant allele can be viewed at once or hidden using the 'show'/'hide' option in the header of this section.

A brief Allele Tour (http://www.informatics.jax.org/faq/Allele_tour.shtml) is available giving an overview of these changes and a help document further explains the Phenotypic Allele Detail pages (http://www.informatics.jax.org/userdocs/allele_detail_report.shtml).

Unified mouse gene catalog

The catalog of mouse genes in MGD serves as the foundation for functional annotation of all genes and genome features in the MGI database. The MGD gene curation process integrates gene predictions from Ensembl, NCBI and Vega into a single, nonredundant catalog. The unified gene catalog for most recent genome assembly (NCBI Build 37, or B37) is available from MGD and is updated when new gene predictions are released.

The concept of gene in the unified mouse gene catalog refers to the computational prediction of structural genome features including protein- and nonprotein-coding genes. The concept of gene in MGD generally includes the additional concept of heritable phenotype. That is, cases where an observable trait appears to be inherited in a typical Mendelian fashion but the underlying structural gene is not known.

Build 37 (B37), which includes ~2.6 GB of mouse sequence, is considered to be 'essentially complete'. MGD has the most current B37 data available from three providers, NCBI, Ensembl and Vega. The MGI Mouse Genome Sequencing group analyzed the files from these three sources to produce a unified mouse gene catalog that established associations between MGI markers and the updated coordinates. This allows researchers to obtain a comprehensive list of mouse genes from a single source and serves as the basis for functional annotation of genes in the MGI database.

The algorithm for our gene 'unification' process has been described previously (9). Rather than relying on sequence similarity to determine the equivalency of predicted genes, our process looks for the genome coordinate overlap of annotated exons. Combining the gene predictions from NCBI, Ensembl and Vega for B37 we produced a catalog of over 34 000 genes and pseudogenes in the mouse genome. Although the overlap of genes predicted by the different groups was significant there are also a large number of genes and pseudogenes that are unique to each of the gene prediction processes. For example, the initial analysis of gene predictions from B37 indicated that 6953 genes were unique to NCBI, 4707 were unique to Ensembl and 2986 were unique to Vega.

New web design and search tool

New web design. Exploring MGI is now assisted with a navigation bar that appears on each web page. The navigation bar features cascading menus that lead users quickly to specific search forms and information pages. The homepage (Figure 3) boasts new major content area images, leading to specific content pages that, in turn, provide relevant data access points and FAQs. This new navigation paradigm improves intuitive navigation of MGI, providing more visual clues for users and allowing quick access to the desired MGI pages.

New search tool. Recently, major infrastructure enhancements have made the MGI Quick Search Tool (Figure 4) a verbose and comprehensive search entrée into MGI data. The Quick Search now combines nomenclature and ID searches with searches of MGI annotations

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Eng^{tm1Mie} Targeted Allele Detail

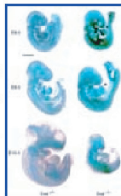
Your Input Welcome

Allele
Symbol: Eng^{tm1Mie}
Name: targeted mutation 1, Michelle Letarte
ID: MGI:2177824

Synonyms
 End -, Eng-

Allele details
Allele Type: Targeted (Reporter)
Strain of Origin: 129P2/OlaHsd
ES Cell Line: E14
Mutation: Disruption caused by insertion of vector
 A lacZ gene and neomycin resistance cassette replaced exon 1. RT-PCR analysis on RNA derived from homozygous embryos demonstrated that no detectable Eng transcript was produced. However, a beta-galactosidase protein was produced from this allele under the control of the endogenous promoter. ([J:58502](#))
Gene Expression in Eng^{tm1Mie} mutants ([7 Assay Results](#))
International Mouse Strain Resource: ([Search for IMSR strains with Eng mutations](#))
Mouse Models of Human Disease: ([See Below](#))
References and Additional Notes: ([See Below](#))

Gene information
Symbol: Eng | **Human Ortholog:** ENG
Name: endoglin
Chromosome: 2:32502115-32538178 bp, + strand | **Genetic Position:** 21.4 cM



Arrest in development in Eng^{tm1Mie}/Eng^{tm1Mie} embryos

Show the [5 image\(s\)](#) involving this allele.

1

Phenotype summary (?)

Phenotype Summary by Mammalian Phenotype terms
 (show or hide all annotated terms)

Genotypes are listed in the next section.

Affected Systems	Genotypes:	hm1	ht2	ht3	ht4
		hm1	ht2	ht3	ht4
cardiovascular system		✓	✓	✓	N
cellular		✓			
craniofacial		✓			
embryogenesis		✓			
growth/size		✓		✓	
homeostasis/metabolism		✓			
lethality/prenatal-perinatal		✓			
life span/aging			✓		
respiratory system		✓		✓	
skin/coat/nails				✓	
Disease Models			✓	✓	

2

Phenotypic data by genotype
 (show or hide all phenotypic details)

Genotype	Allelic Composition	Genetic Background
▶ hm1	Eng ^{tm1Mie} /Eng ^{tm1Mie}	involves: 129P2/OlaHsd * C57BL/6
▶ ht2 <i>Disease Model</i>	Eng ^{tm1Mie} /Eng ⁺	129P2/OlaHsd-Eng ^{tm1Mie}
▶ ht3 <i>Disease Model</i>	Eng ^{tm1Mie} /Eng ⁺	involves: 129P2/OlaHsd * C57BL/6
▶ ht4	Eng ^{tm1Mie} /Eng ⁺	involves: 129P2/OlaHsd * C57BL/6 * CD-1

2

Disease models

Mouse Models of Human Disease	Note	Genotype		Ref(s)
		Allelic Composition	Genetic Background	
Models with phenotypic similarity to human diseases associated with human ENG.				
Telangiectasia, Hereditary Hemorrhagic, of Rendu, Osler, and Weber; OMIM ID: 187300		ht3	Eng ^{tm1Mie} /Eng ⁺	involves: 129P2/OlaHsd * C57BL/6 J:58502
		ht2	Eng ^{tm1Mie} /Eng ⁺	129P2/OlaHsd-Eng ^{tm1Mie} J:58502

2

References
 (Original) [J:58502](#) Bourdeau A et al., "A murine model of hereditary hemorrhagic telangiectasia [see comments]" J Clin Invest 1999 Nov;104(10):1343-51
[All references\(11\)](#)

Figure 1. Allele detail page for the Eng^{tm1Mie} targeted mutation. The 'Phenotype summary' section [labeled 1] displays a matrix view of phenotype terms (vertical axis) by genotypes (horizontal axis). Phenotype terms can be expanded to show more detail and each genotype abbreviation links to a page detailing the full phenotype for that genotype. The 'Phenotypic data by genotype' section [labeled 2] shows a table of genotypes involving Eng^{tm1Mie}. Each genotype can be expanded to reveal full phenotypes. All data for each of the phenotype sections of this page can be viewed using the 'show'/'hide' options in the section headers.

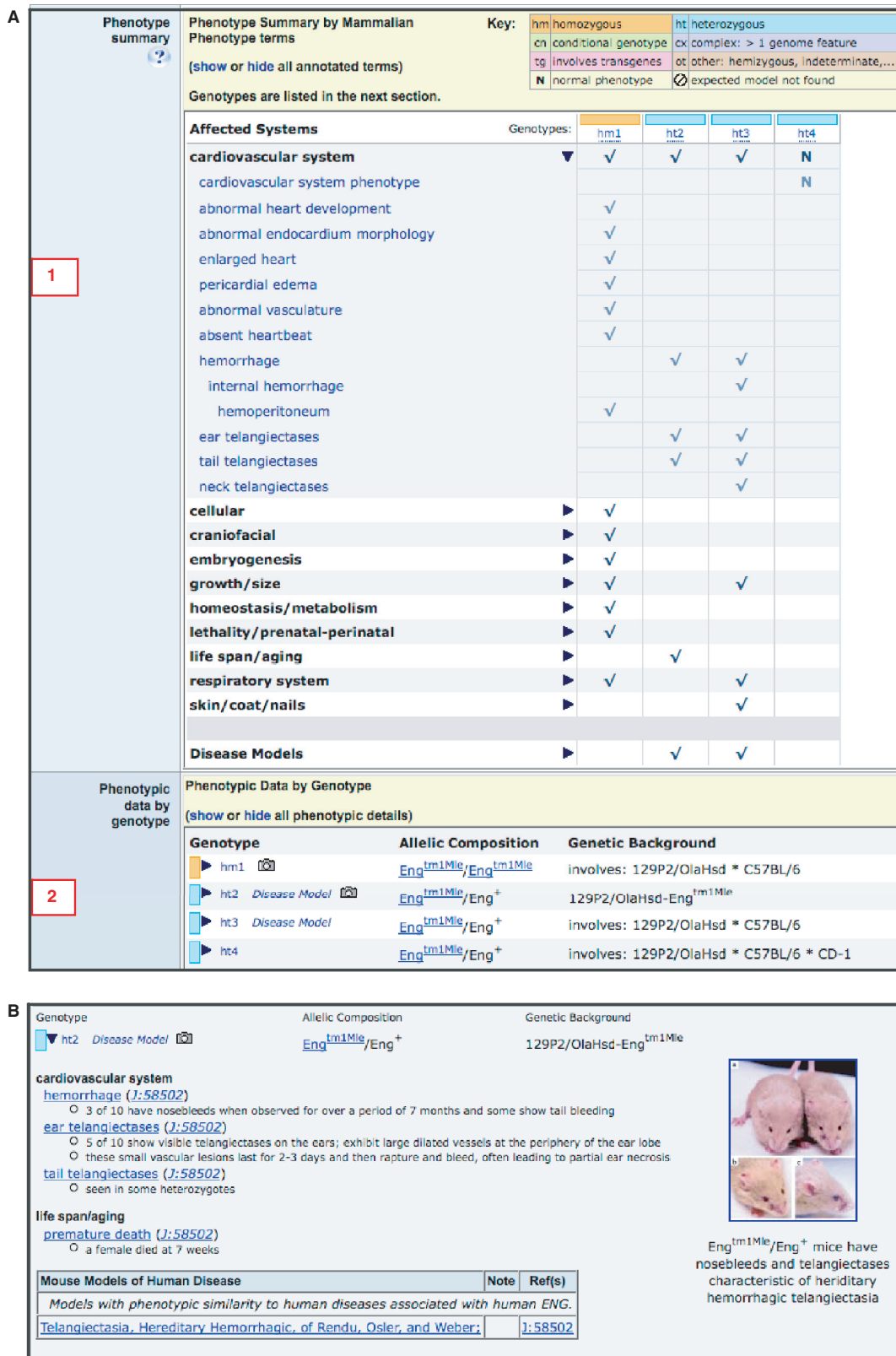


Figure 2. Using the new expansion features for comparing phenotypes. (A) The ‘Phenotype summary’ matrix is shown expanded for the cardiovascular system term [labeled 1]. Note the finer granularity of the terms. The genetic background effect in $Eng^{tm1Mie}/+$ heterozygotes can clearly be seen. Heterozygote 4 (ht4) displays a normal cardiovascular phenotype, compared with the other two heterozygous genotypes (ht2, ht3). By glancing below to the ‘Phenotypic data by genotype’ section [labeled 2], it can be observed that in $Eng^{tm1Mie}/+$ mice, the addition of background alleles from the CD-1 strain appears to confer a protective effect for these cardiovascular system phenotypes. (B) The ‘Phenotypic data by genotype’ section is shown expanded for one of the genotypes ($Eng^{tm1Mie}/+$ heterozygotes in the 129P2/OlaHsd- Eng^{tm1Mie} strain, abbreviated ht2).

MGI [Tour the MGI website](#) [Quick Search](#)

Mouse Genome Informatics

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Explore MGI [All Search Tools](#)

Genes

Phenotypes

Expression

Function

Pathways

Strains / SNPs

Variation Type	DBV/ZJ	FVB/NJ	PAU/VEJ	Allele Summary (all strains)
SNP	G	G	A	A/G
SNP	C	C	T	C/T

Orthology

Tumors

FAQs

How do I...

- .. search for genes? [FAQ](#)
- .. find mutations for phenotypes or diseases? [FAQ](#)
- .. find expression data? [FAQ](#)
- .. view a structural genomic map? [FAQ](#)

[More FAQs](#)

News 18 September, 2008

- MGI release 4.12 features a new **Phenotype summary** section on allele detail pages, allowing easy comparisons of phenotypes across genotypes. [Read more...](#)
- The MGI 4.11 release includes enhancements related to gene expression data. [Read more...](#)
- MGI genome coordinates are now [updated](#) to NCBI Mouse Build 37 and dbSNP Build 128.

[More MGI news](#) [MGI Statistics](#)

Mouse Community News

MGI Roadshow:

- 10/8 [University of Colorado Health Sciences Center](#)
- 10/16 [Stanford University](#)
- 10/17 [University of California Berkeley](#)
- 10/30-31 [Ontario Genomics Institute](#)
- 11/4 [UNC Chapel Hill](#)
- 11/5 [Duke University](#)
- 11/5 [North Carolina State University](#)

If you would like to host a MGI workshop at your institution, contact [User Support](#) to discuss the details.

Visit MGI posters at these upcoming conferences:

- [3rd ESF Conference on Functional Genomics and Disease](#)
- [8th IEEE International Conference on Bioinformatics and BioEngineering \(BIBE2008\)](#)
- [Mouse Genetics & Genomics: Development & Disease](#)
- [22nd International Mammalian Genome Conference \(IMGC\)](#)

Read about the International Mouse Knockout Consortium [KOMP (USA); EUCOMM (Europe); NorCOMM (Canada); TIGM (USA)] in *Cell* 2007; 128: 9-13, PMID: [17218247](#) and *Cell* 2007; 129: 235, PMID: [17448981](#).

See MGI's collection of mouse resources and model organism links.

Figure 3. Redesigned MGI Homepage. Notable design items of the new MGI web pages include a navigation bar that is included on every MGI page, featuring cascading menus that lead users quickly to the query form or information page of interest. On the homepage, clickable images representing major content areas lead users to pages with additional information, descriptions of MGD data for that area, links to query forms and reports, and relevant FAQs.

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Quick Search Results

for: Search Again Reset

Examples: embryo* develop* NM_013627 Lep<ob> Pax* axial "skeletal dysplasia" T(XA1?;IN)8EI

Genome Features

sorted by best match, showing 1-10 of 1,931

Score	Type	Symbol	Name	Chr	Best Match
<input type="checkbox"/>	Gene	Pax6	paired box gene 6	2	ID : NM_013627 (RefSeq) more..
<input type="checkbox"/>	Gene	Acan	aggrecan	7	PHENOTYPE : deafness more..
<input type="checkbox"/>	Gene	Accn1	amiloride-sensitive cation channel 1, neuronal (degenerin)	11	FUNCTION : hearing more..
<input type="checkbox"/>	Gene	Alms1	Alstrom syndrome 1 homolog (human)	6	FUNCTION : hearing more..
<input type="checkbox"/>	Gene	Apoe	apolipoprotein E	7	PHENOTYPE : deafness more..
<input type="checkbox"/>	Gene	Aqp4	aquaporin 4	18	PHENOTYPE : deafness more..
<input type="checkbox"/>	Gene	Arsa	arylsulfatase A	15	PHENOTYPE : deafness more..
<input type="checkbox"/>	Gene	Atp2b2	ATPase, Ca++ transporting, plasma membrane 2	6	PHENOTYPE : deafness more..
<input type="checkbox"/>	Gene	Atp6v1b1	ATPase, H+ transporting, lysosomal V1 subunit B1	6	FUNCTION : hearing more..
<input type="checkbox"/>	Gene	Axin1	axin 1	17	PHENOTYPE : deafness more..

[Show first 100...](#) Get more data for genome features 1 through in [Web Format](#) [Tab Format](#)

Vocabulary Terms

sorted by best match, showing 1-10 of 307

Score	Term	Associated Data	Best Match
<input type="checkbox"/>	PHENOTYPE : deafness	164 genotypes, 164 annotations	TERM : deafness
<input type="checkbox"/>	FUNCTION : sensory perception of sound	92 genes, 106 annotations	SYNONYM : hearing
<input type="checkbox"/>	DISEASE : Alport Syndrome, Autosomal Dominant	1 mouse model	SYNONYM : Nephropathy and Deafness
<input type="checkbox"/>	DISEASE : Alport Syndrome, Autosomal Recessive	5 mouse models, 1 mouse ortholog	SYNONYM : Nephropathy and Deafness
<input type="checkbox"/>	DISEASE : Deafness, Unilateral		TERM : Deafness, Unilateral
<input type="checkbox"/>	DISEASE : Deafness, X-Linked 2; DFNX2	8 mouse models	SYNONYM : Nance Deafness
<input type="checkbox"/>	DISEASE : Diabetes-Deafness Syndrome, Maternally Transmitted		SYNONYM : Niddm with Deafness
<input type="checkbox"/>	DISEASE : Pendred Syndrome; PDS	4 mouse models	SYNONYM : Deafness with Goiter
<input type="checkbox"/>	DISEASE : Tune Deafness		TERM : Tune Deafness
<input type="checkbox"/>	PHENOTYPE : impaired hearing	228 genotypes, 257 annotations	SYNONYM : hearing loss

[Show first 100...](#)

Other Results Matched By ID

sorted by best match, showing 1-1

Type	Name/Description	Why did this match?
Sequence, RNA	Mus musculus paired box gene 6 (Pax6), mRNA.	ID : NM_013627 (RefSeq)

Search MGI with Google

Figure 4. New MGI search tool. The new search tool provides maximum flexibility for quickly locating genes and annotations of interest in MGI. Searches are automatically done against nomenclature (gene symbols/names, synonyms, orthologs), ontologies/vocabularies used for MGI data associations, including gene function, process and cellular location (GO), phenotype (MP) and disease terms (OMIM), anatomical terms, protein domains (PIRSF) and accession IDs. Results returned are ranked by best match to the term(s) entered by the user and links are provided to the underlying data and to a comprehensive list of matches in the database. The figure shows the results for searching for: deafness hearing NM_013627. The terms deafness and/or hearing were matched to 267 genes and 246 vocabulary terms, and the sequence ID retrieved the corresponding RefSeq match.

and ontologies. The combination of an enhanced nomenclature search (symbols, names, orthologs), and complete indexing of MGI data, and weighted word searches provides an instantaneous return of information, as well as data for the user on the nature of the returned object. The Quick Search has become a robust way for those unfamiliar with MGI to focus their interests and a simplified search for users who seek quick entry into specific information (e.g. give me detail for gene X; what information does MGI have about retinal degeneration?). Advanced search forms in MGI continue to support complex queries

such as ‘What genes on Chromosome 11 functions as transcription factors and have mutations associated with abnormalities of the inner ear?’

COMMUNITY AUTHORITIES AND ACCESS

Mouse gene, allele and strain nomenclature

MGD is responsible for assigning official nomenclature to mouse genes, alleles and strains following the guidelines set by the International Committee on Standardized

Genetic Nomenclature for Mice (<http://www.informatics.jax.org/nomen>). MGD staff work with various bioinformatics resource curators to resolve nomenclature inconsistencies resulting from regular data exchange of shared links, and with specialists for human (<http://www.genenames.org/>), rat (<http://rgd.mcw.edu>) and other species (e.g. zebrafish <http://zfin.org>) to provide an organized approach to the nomenclature process. Collaborative efforts between the mouse and human nomenclature committees and scientific experts in specific domain areas provide an up-to-date analysis and compilation of the latest knowledge about genes and gene families, such as the NLR family (10). The MGD group that also assists journal editors to ensure standardized nomenclature is adhered to in publications. The MGD nomenclature coordinator can be contacted by email (nomen@informatics.jax.org).

Electronic data submission

MGD accepts contributed data sets for any type of data maintained by the database. The most frequent types of contributed data are mutant allele and phenotypic information originating with the large mouse mutagenesis centers and repositories that contribute to the International Mouse Strain Resource (IMSR, <http://www.imsr.org>). Each electronic submission receives a permanent database accession ID. All data sets are associated with their source, either a publication or an electronic submission reference. Online details about data submission procedures is found at http://www.informatics.jax.org/mgi_home/submissions/submissions_menu.shtml.

Community outreach and user support

MGD user support can be accessed through online documentation and easy email or phone access to User Support Staff.

- World Wide Web: http://www.informatics.jax.org/mgi_home/support/support.shtml
- Email access: mgi-help@informatics.jax.org
- Telephone access: 1-207-288-6445
- FAX access: 1-207-288-6132

Other outreach: MGI-LIST (<http://www.informatics.jax.org/mgihome/lists/lists.shtml>) is a moderated and active email bulletin board supported by the MGD User Support group.

HIGH-LEVEL OVERVIEW OF THE MAIN COMPONENTS AND IMPLEMENTATION

MGD is implemented in the Sybase relational database management system with approximately 180 tables within which the biological information is stored. BLAST-able databases, genome assembly files for sequence data and image data are stored outside the relational database. An editing interface (EI) and automated load programs are used to input data into the MGD system. The EI is an interactive, graphical application used by curators. Automated load programs that integrate larger data sets from many sources into the database

include quality control (QC) checks and processing algorithms that integrate the bulk of the data automatically and identify issues to be resolved by curators or the data provider. Thus, through EI and automated loads, we acquire and integrate large amounts of data into a high-quality, knowledgebase.

Public data access is provided through the web interface (WI) where users can interactively query and download our data through a web browser. MouseBLAST allows users to do sequence similarity searches against a variety of rodent-relevant sequence databases that are built weekly from selected sequence databases from NCBI, UniProt and other providers. Mouse GBrowse allows users to visualize mouse data sets against the genome as a series of linear tracks. FTP reports are a major source for other data providers who link to or use MGD data in their products, and for computational biologists who use MGD data in their analyses. Programmatic access to MGD via web services is also available. All MGD files and programs are openly and freely available.

CITING MGD

For a general citation of the MGD resource please cite this article. In addition, the following citation format is suggested when referring to datasets specific to the MGD component of MGI: Mouse Genome Database (MGD), Mouse Genome Informatics, The Jackson Laboratory, Bar Harbor, Maine (URL: <http://www.informatics.jax.org>). [Type in date (month, year) when you retrieved the data cited.] Citation, Copyright, Warranty Disclaimer and other resource-specific information can be found in the footer of all MGI web pages.

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