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The Mouse Genome Database (MGD): updates and enhancements

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ABSTRACT

The Mouse Genome Database (MGD) integrates genetic and genomic data for the mouse in order to facilitate the use of the mouse as a model system for understanding human biology and disease processes. A core component of the MGD effort is the acquisition and integration of genomic, genetic, functional and phenotypic information about mouse genes and gene products. MGD works within the broader bioinformatics community to define referential and semantic standards to facilitate data exchange between resources including the incorporation of information from the biomedical literature. MGD is also a platform for computational assessment of integrated biological data with the goal of identifying candidate genes associated with complex phenotypes. MGD is web accessible at http://www.informatics.jax.org. Recent improvements in MGD described here include the incorporation of an interactive genome browser, the enhancement of phenotype resources and the further development of functional annotation resources.

INTRODUCTION

The Mouse Genome Database (MGD) provides a comprehensive and integrated view of genetic, genomic and biological information for the laboratory mouse (1,2). The primary mission of MGD is to facilitate the use of the laboratory mouse as a model for studying human biology and disease. MGD contains information on mouse genes, genetic markers and genomic features and includes comprehensive information for these features including sequence sets, mapping details, Gene Ontology (GO) annotations, allele descriptions and mutant phenotype characteristics (Table 1). MGD integrates sequence with biology through the curated association of genome, transcript and protein sequence sets with mouse genes, and work done in collaboration with other large genome informatics resources. A primary goal of MGD is to be the hub for mouse phenotype information and to provide robust access to phenotypic data for human users and for computational applications.

MGD is updated daily and there are weekly data exchanges with other major genomics resources, such as NCBI and UniProt. A recent snapshot of MGD content is shown in Table 1. MGD continues to evolve, expanding its data coverage, improving data access, and providing new data query, analysis and display tools. Current efforts focus on the incorporation of genome visualization tools and the explicit representation of mouse models in the context of their relationship to human disease presentations.

Table 1. Snapshot of data content in MGD: September 12, 2005

MGD data statistics	September 12, 2005
Number of genes with sequence data	27 617
Number of genes (incl. unmapped mutants)	30 881
Number of markers (including genes)	57 368
Number of markers mapped	53 212
Number of genes with protein sequence information	19 580
Number of genes with GO annotations	16 572
Number of mouse/human orthologies	15 849
Number of mouse/rat orthologies	15 532
Number of genes with one or more phenotypic alleles	6191
Number of cataloged phenotypic alleles	14 338
Number of references	94 891
Number of mouse nucleotide sequences integrated into the MGI system (includes expressed sequence tags)	>7 600 000

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MGD is a core component of the Mouse Genome Informatics (MGI) database resource (http://www.informatics.jax.org) hosted at The Jackson Laboratory (http://www.jax.org). Other projects and resources that are part of the MGI system include the Gene Expression Database (GXD) (3) (http://www.informatics.jax.org/mgihome/GXD/aboutGXD.shtml) and the Mouse Tumor Biology Database (MTB) (4) (http://tumor.informatics.jax.org). All MGI component groups participate actively in the development and application of the Gene Ontology (GO) (5) (http://www.geneontology.org).

IMPROVEMENTS DURING 2004

Implementation of Mouse Genome Browser

A mouse implementation of the Generic Genome Browser (6) has been installed at MGD. A number of unique MGD tracks are available on the Mouse GBrowse (http://gbrowse.informatics.jax.org/cgi-bin/gbrowse/mouse_build_34), including MGI representative transcripts, SNPs, alleles, QTLs and phenotype annotations (Figure 1). Also available are the Ensembl and NCBI genome annotation, GenBank mouse mRNAs and STS markers. GBrowse is also used to generate thumbnail images of the intron–exon structure of genes on the MGD gene detail pages. GBrowse allows users to upload their own genome annotations to be viewed in the context of existing annotation tracks. GBrowse is accessible from the MGI home pages as well as from Gene Detail pages.

Enhanced representation of relationship between mouse models and human diseases

For some time, MGD curators have associated mouse mutant alleles with OMIM, a text-based compendium of human genes and diseases maintained by the Johns Hopkins University (7). This was accomplished by inserting simple hypertext links into mouse mutant allele descriptions where mice carrying these alleles had been reported as disease models. These links were not searchable and could be viewed only at the level of the allele description.

We have made these more explicit to show the relationship between the actual mouse genotype and the human disease it models. We have added OMIM disease terms to MGD as a vocabulary to allow users to access these data from a human-centric as well as a mouse-centric view (Figure 2). The vocabulary of OMIM disease terms is stored and maintained in the same way as the other controlled vocabularies (GO, Anatomy, etc.). Currently, 5920 OMIM terms are contained in MGD and loads are refreshed nightly.

New presentation of Gene Ontology annotations

We have responded to biologists' requests to provide functional annotation information in human-readable form by providing Gene Ontology annotations in a templated text representation (Figure 3). A lexicon of grammar rules and templates provides the structure for the automated construction of the GO text from the GO annotation files. Users may view GO annotations via their web browsers either as text or in a tabular presentation. Presently, the text presentation is updated weekly, whereas the data in the tables are updated daily. We will continue to improve the text generation scripts to incorporate paragraphs generated from other structured data in MGD.

OTHER ACTIVITIES OF NOTE IN 2005

Harmonization of mouse and rat nomenclatures. MGD initiated the merging of mouse and rat gene, allele and strain nomenclature guidelines via the Committee for Standardized Nomenclature in Mice and the Rat Genome and Nomenclature Committee. There is now a common standard for nomenclatures in rodent species that provides a simplified system for researchers and should lessen the redundancy of names of strains in mice and rats and encourage the co-naming of gene orthologs.

FANTOM 3 data loads. MGD staff have participated in each of the three FANTOM (Functional Annotation of the Mouse) projects as part of a consortium working to curate a large cDNA clone sequences. The FANTOM 3 project provides a comprehensive view of the transcriptional landscape of the mouse genome (8). More than 100 000 cDNA clone sequences have been released to date by the FANTOM consortium and they have been integrated into MGD.

Electronic publication. We now have posted an electronic publication of *The Anatomy of the Laboratory Mouse* by Margaret J. Cook. This out-of-print book is a classic anatomy text first published in 1965. This book joins other out-of-print classics of mouse genetics in electronic publication at MGD.

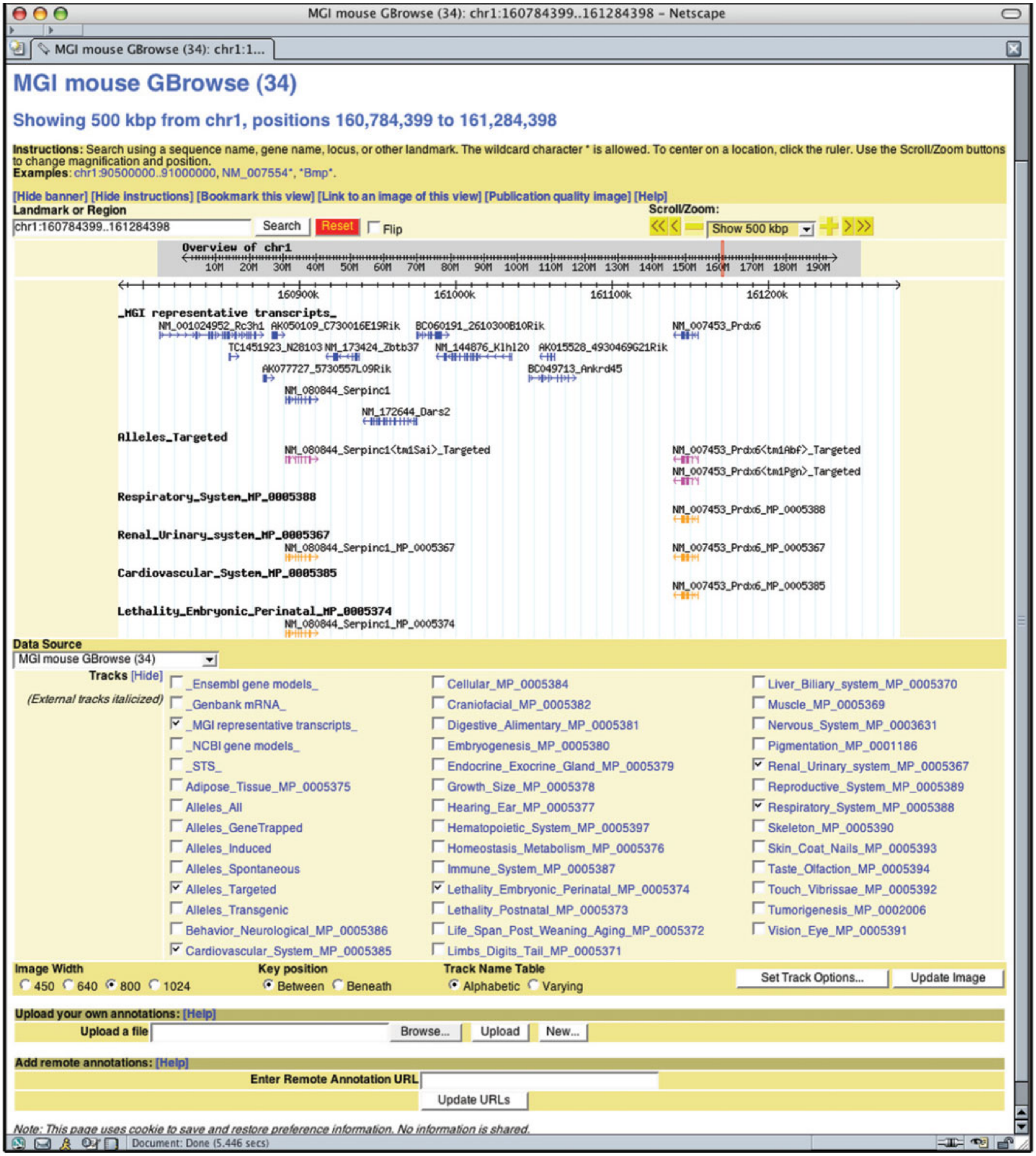
OTHER INFORMATION

Mouse gene nomenclature

The MGD gene annotation group assigns unique symbols and names to mouse genes under the guidelines set by the *International Committee on Standardized Genetic Nomenclature for Mice* (http://www.informatics.jax.org/mgihome/nomen/index.shtml). Through curation of shared links between MGI and other bioinformatics resources, the official nomenclature for mouse genes is becoming widely disseminated. The MGI nomenclature group works closely with nomenclature specialists for human (http://www.gene.ucl.ac.uk/cgi-bin/nomenclature/searchgenes.pl) and rat (http://rgd.mcw.edu) to provide consistent nomenclature for mammalian species. The mouse and human nomenclature committees collaborate with scientists prominent in a specialist area to develop a nomenclature scheme for those genes that should be grouped together in a family, such as the ARID family (10) or to revise the nomenclature for an already established gene family, such as the ACOT family (11). Scientists can contact the MGD nomenclature coordinator by email (nomen@informatics.jax.org) and can reserve symbols prior to publication using the electronic nomenclature submission form (http://www.informatics.jax.org/mgihome/nomen/nomen_submit_form.shtml).

Electronic data submission

Any type of data that MGD maintains can be submitted as an electronic contribution. Over the last year, the most frequent



MGI mouse GBrowse (34): chr1:160784399..161284398 – Netscape

MGI mouse GBrowse (34): chr1:1...

MGI mouse GBrowse (34)

Showing 500 kbp from chr1, positions 160,784,399 to 161,284,398

Instructions: Search using a sequence name, gene name, locus, or other landmark. The wildcard character * is allowed. To center on a location, click the ruler. Use the Scroll/Zoom buttons to change magnification and position.
Examples: chr1:90500000..91000000, NM_007554*, *Bmp*.

[Hide banner] [Hide instructions] [Bookmark this view] [Link to an image of this view] [Publication quality image] [Help]

Landmark or Region: chr1:160784399..161284398 Search Reset □ Flip

Scroll/Zoom: Show 500 kbp

Overview of chr1
10M
20M
30M
40M
50M
60M
70M
80M
90M
100M
110M
120M
130M
140M
150M
160M
170M
180M
190M
160900k
161000k
161100k
161200k
MGI representative transcripts
NM_001024952_Rc3h1
AK050109_C730016E19Rik
BC060191_2610300B10Rik
NM_007453_Prdx6
TC1451923_N28103
NM_173424_Zbtb37
NM_144876_Klhl20
AK015528_4930469G21Rik
AK077727_5730557L09Rik
BC049713_Ankrd45
NM_080844_Serpinc1
NM_172644_Dars2
Alleles_Targeted
NM_080844_Serpinc1<tm1Sai>_Targeted
NM_007453_Prdx6<tm1Abf>_Targeted
NM_007453_Prdx6<tm1Pgn>_Targeted
Respiratory_System_MP_0005388
NM_007453_Prdx6_MP_0005388
Renal_Urinary_system_MP_0005367
NM_080844_Serpinc1_MP_0005367
NM_007453_Prdx6_MP_0005367
Cardiovascular_System_MP_0005385
NM_007453_Prdx6_MP_0005385
Lethality_Embryonic_Perinatal_MP_0005374
NM_080844_Serpinc1_MP_0005374

Data Source MGI mouse GBrowse (34)

Tracks [Hide]
(External tracks italicized)

- □ _Ensembl gene models_
- □ _Genbank mRNA_
- ☑ _MGI representative transcripts_
- □ _NCBI gene models_
- □ _STS_
- □ Adipose_Tissue_MP_0005375
- □ Alleles_All
- □ Alleles_GeneTrapped
- □ Alleles_Induced
- □ Alleles_Spontaneous
- ☑ Alleles_Targeted
- □ Alleles_Transgenic
- □ Behavior_Neurological_MP_0005386
- ☑ Cardiovascular_System_MP_0005385
- □ Cellular_MP_0005384
- □ Craniofacial_MP_0005382
- □ Digestive_Alimentary_MP_0005381
- □ Embryogenesis_MP_0005380
- □ Endocrine_Exocrine_Gland_MP_0005379
- □ Growth_Size_MP_0005378
- □ Hearing_Ear_MP_0005377
- □ Hematopoietic_System_MP_0005397
- □ Homeostasis_Metabolism_MP_0005376
- □ Immune_System_MP_0005387
- ☑ Lethality_Embryonic_Perinatal_MP_0005374
- □ Lethality_Postnatal_MP_0005373
- □ Life_Span_Post_Weaning_Aging_MP_0005372
- □ Limbs_Digits_Tail_MP_0005371
- □ Liver_Biliary_system_MP_0005370
- □ Muscle_MP_0005369
- □ Nervous_System_MP_0003631
- □ Pigmentation_MP_0001186
- ☑ Renal_Urinary_system_MP_0005367
- □ Reproductive_System_MP_0005389
- ☑ Respiratory_System_MP_0005388
- □ Skeleton_MP_0005390
- □ Skin_Coat_Nails_MP_0005393
- □ Taste_Olfaction_MP_0005394
- □ Touch_Vibrissae_MP_0005392
- □ Tumorigenesis_MP_0002006
- □ Vision_Eye_MP_0005391

Image Width ○ 450 ○ 640 ● 800 ○ 1024
Key position ● Between ○ Beneath
Track Name Table ● Alphabetic ○ Varying

Set Track Options... Update Image

Upload your own annotations: [Help]
Upload a file Browse... Upload New...

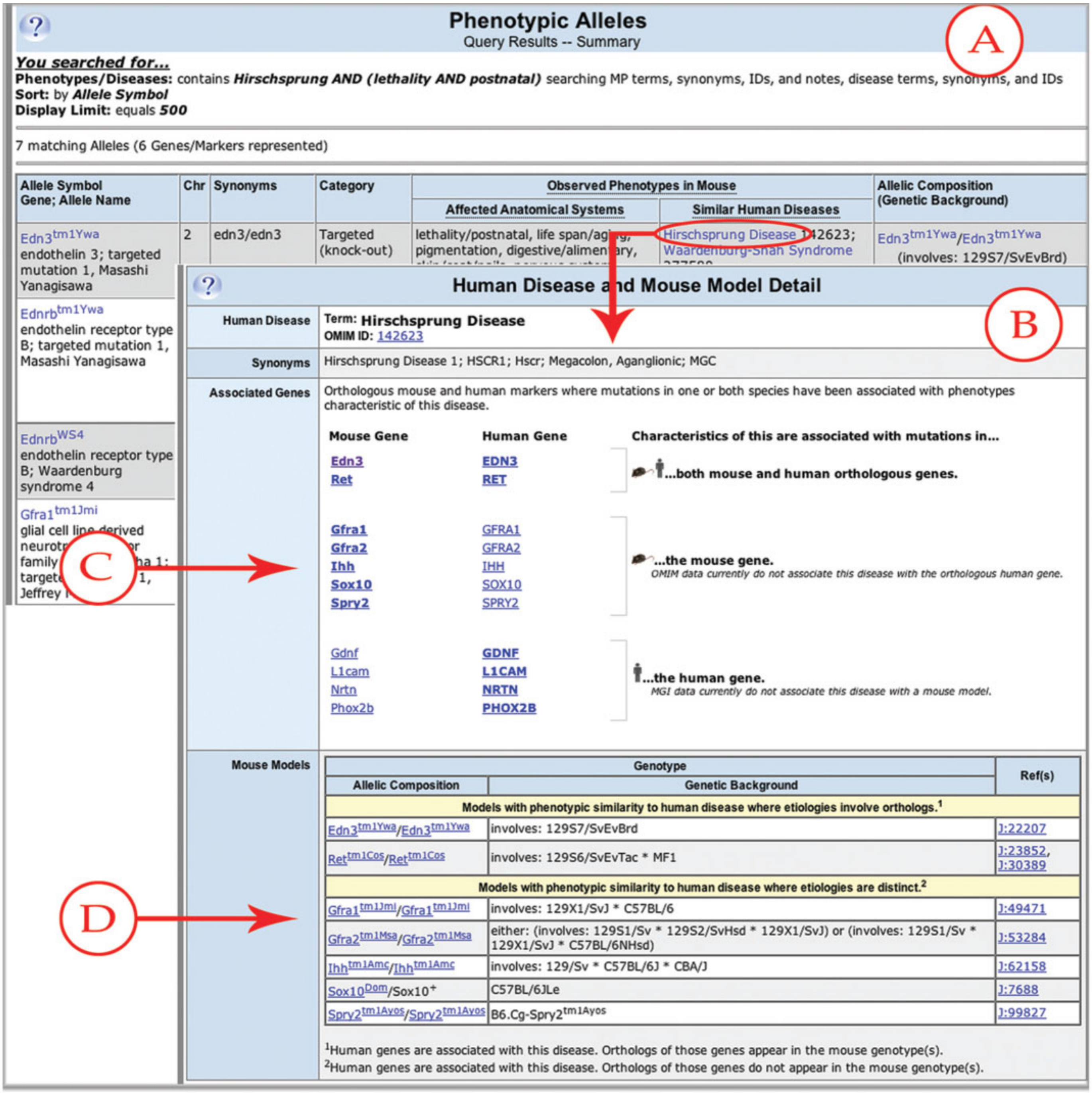
Add remote annotations: [Help]
Enter Remote Annotation URL
Update URLs

Note: This page uses cookie to save and restore preference information. No information is shared.

Document: Done (5.446 secs)

Figure 1. Mouse GBrowse: a screen shot of the MGI Mouse GBrowse interface. Using Mouse GBrowse, users can display MGD-specific annotations about genes, allele types (e.g. spontaneous, targeted, transgenic, etc.) and phenotype to gene associations. Each glyph displayed in the browser is hypertext linked to the appropriate detail page in MGD. Particularly note the phenotype tracks.

submissions have been of mutant and phenotypic allele information originating with the large mouse mutagenesis centers. Other common types of submission include mutant and QTL mapping data. Each electronic submission receives a permanent database accession ID. All datasets are associated with either a publication or an electronic submission reference. MGD reference pages provide links to associated datasets. On-line information about data submission



Phenotypic Alleles
Query Results -- Summary

You searched for...
Phenotypes/Diseases: contains ***Hirschsprung AND (lethality AND postnatal)*** searching MP terms, synonyms, IDs, and notes, disease terms, synonyms, and IDs
Sort: by ***Allele Symbol***
Display Limit: equals ***500***

7 matching Alleles (6 Genes/Markers represented)

Allele Symbol Gene; Allele Name	Chr	Synonyms	Category	Observed Phenotypes in Mouse		Allelic Composition (Genetic Background)
				Affected Anatomical Systems	Similar Human Diseases	
Edn3^{tm1Ywa} endothelin 3; targeted mutation 1, Masashi Yanagisawa	2	edn3/edn3	Targeted (knock-out)	lethality/postnatal, life span/ag, pigmentation, digestive/alimentary,	Hirschsprung Disease 142623; Waardenburg-Shah Syndrome	Edn3^{tm1Ywa}/Edn3^{tm1Ywa} (involves: 129S7/SvEvBrd)
Ednrb^{tm1Ywa} endothelin receptor type B; targeted mutation 1, Masashi Yanagisawa						
Ednrb^{WS4} endothelin receptor type B; Waardenburg syndrome 4						
Gfra1^{tm1Jmi} glial cell line derived neurotr or family ha 1: targete 1, Jeffrey						

Human Disease and Mouse Model Detail

Human Disease — **Term: Hirschsprung Disease**
OMIM ID: 142623

Synonyms — Hirschsprung Disease 1; HSCR1; Hscr; Megacolon, Aganglionic; MGC

Associated Genes — Orthologous mouse and human markers where mutations in one or both species have been associated with phenotypes characteristic of this disease.

Mouse Gene	Human Gene	Characteristics of this are associated with mutations in...
Edn3 Ret	EDN3 RET	**...both mouse and human orthologous genes.**
Gfra1 Gfra2 Ihh Sox10 Spry2	GFRA1 GFRA2 IHH SOX10 SPRY2	**...the mouse gene.** *OMIM data currently do not associate this disease with the orthologous human gene.*
Gdnf L1cam Nrtn Phox2b	GDNF L1CAM NRTN PHOX2B	**...the human gene.** *MGI data currently do not associate this disease with a mouse model.*

Mouse Models

Genotype		Ref(s)
Allelic Composition	Genetic Background	
Models with phenotypic similarity to human disease where etiologies involve orthologs.[1]		
Edn3^{tm1Ywa}/Edn3^{tm1Ywa}	involves: 129S7/SvEvBrd	J:22207
Ret^{tm1Cos}/Ret^{tm1Cos}	involves: 129S6/SvEvTac * MF1	J:23852, J:30389
Models with phenotypic similarity to human disease where etiologies are distinct.[2]		
Gfra1^{tm1Jmi}/Gfra1^{tm1Jmi}	involves: 129X1/SvJ * C57BL/6	J:49471
Gfra2^{tm1Msa}/Gfra2^{tm1Msa}	either: (involves: 129S1/Sv * 129S2/SvHsd * 129X1/SvJ) or (involves: 129S1/Sv * 129X1/SvJ * C57BL/6NHsd)	J:53284
Ihh^{tm1Amc}/Ihh^{tm1Amc}	involves: 129/Sv * C57BL/6J * CBA/J	J:62158
Sox10^{Dom}/Sox10^{+}	C57BL/6JLe	J:7688
Spry2^{tm1Ayos}/Spry2^{tm1Ayos}	B6.Cg-Spry2^{tm1Ayos}	J:99827

[1] Human genes are associated with this disease. Orthologs of those genes appear in the mouse genotype(s).
[2] Human genes are associated with this disease. Orthologs of those genes do not appear in the mouse genotype(s).

Figure 2. Mouse models and human diseases. Panel A: Search summary page of phenotypic alleles indicating observed phenotypes in mouse. The human diseases given in the column 'Similar human diseases' link to the page describing the relationship of this human disease to mouse (Panel B). Panel B: Detail page of human disease and mouse models for Hirschsprung disease. The associated gene section (arrow C) shows where orthologous mouse and human genes have been associated with this disease phenotype. The mouse models section (arrow D) specifies the genotypes of mouse models for this disease that have etiologies involving orthologs or etiologies which are distinct.

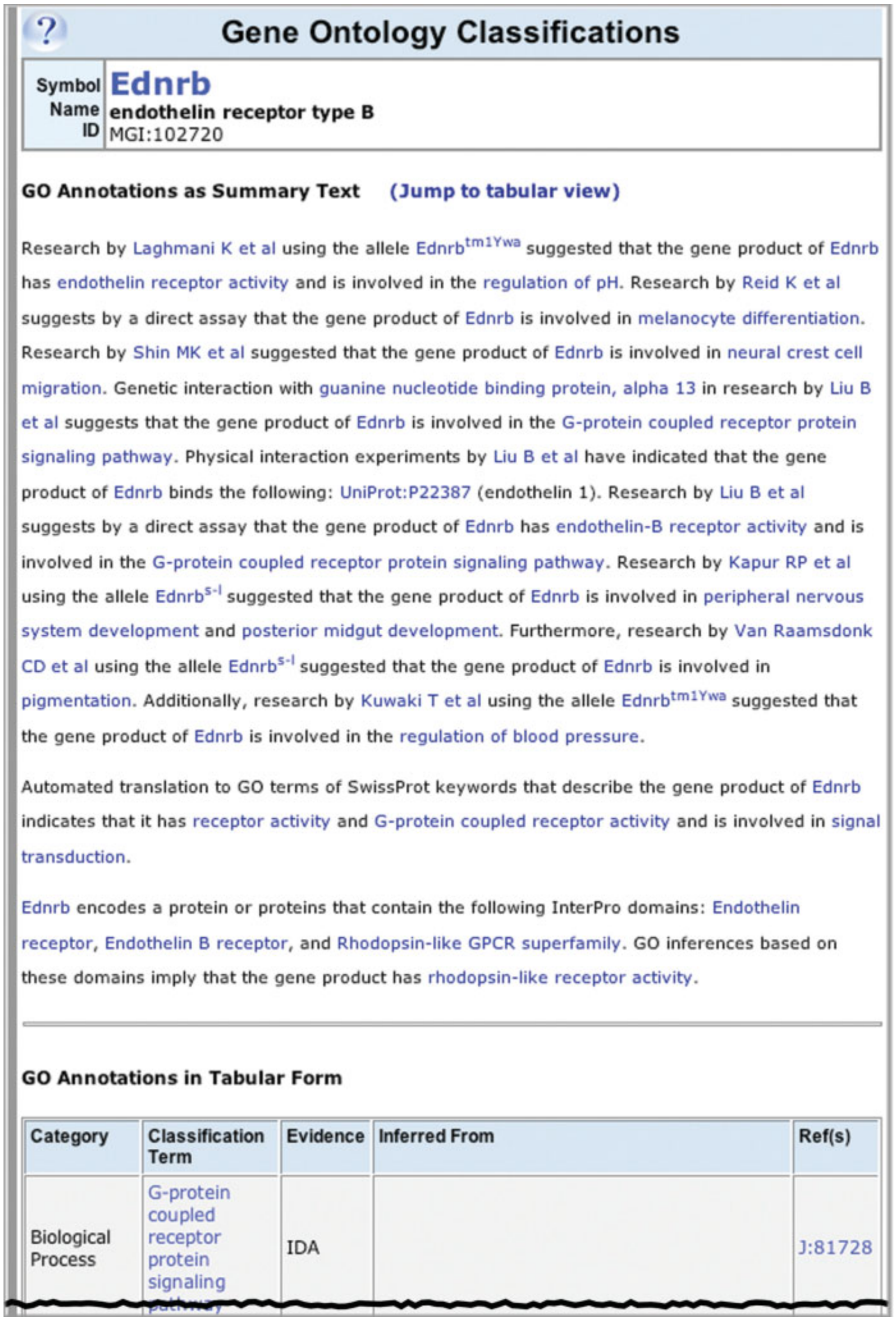
procedures is found at http://www.informatics.jax.org/mgihome/submissions/submissions_menu.shtml.

Community outreach and user support

MGD provides extensive user support through on-line documentation and easy email or phone access to User Support Staff. User Support WWW access: http://www.informatics.jax.org/mgihome/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 MGI Users Support group.



Gene Ontology Classifications

Symbol	Ednrb
Name	endothelin receptor type B
ID	MGI:102720

GO Annotations as Summary Text (Jump to tabular view)

Research by Laghmani K et al using the allele Ednrb^{tm1Ywa} suggested that the gene product of Ednrb has endothelin receptor activity and is involved in the regulation of pH. Research by Reid K et al suggests by a direct assay that the gene product of Ednrb is involved in melanocyte differentiation. Research by Shin MK et al suggested that the gene product of Ednrb is involved in neural crest cell migration. Genetic interaction with guanine nucleotide binding protein, alpha 13 in research by Liu B et al suggests that the gene product of Ednrb is involved in the G-protein coupled receptor protein signaling pathway. Physical interaction experiments by Liu B et al have indicated that the gene product of Ednrb binds the following: UniProt:P22387 (endothelin 1). Research by Liu B et al suggests by a direct assay that the gene product of Ednrb has endothelin-B receptor activity and is involved in the G-protein coupled receptor protein signaling pathway. Research by Kapur RP et al using the allele Ednrb^{s-l} suggested that the gene product of Ednrb is involved in peripheral nervous system development and posterior midgut development. Furthermore, research by Van Raamsdonk CD et al using the allele Ednrb^{s-l} suggested that the gene product of Ednrb is involved in pigmentation. Additionally, research by Kuwaki T et al using the allele Ednrb^{tm1Ywa} suggested that the gene product of Ednrb is involved in the regulation of blood pressure.

Automated translation to GO terms of SwissProt keywords that describe the gene product of Ednrb indicates that it has receptor activity and G-protein coupled receptor activity and is involved in signal transduction.

Ednrb encodes a protein or proteins that contain the following InterPro domains: Endothelin receptor, Endothelin B receptor, and Rhodopsin-like GPCR superfamily. GO inferences based on these domains imply that the gene product has rhodopsin-like receptor activity.

GO Annotations in Tabular Form

Category	Classification Term	Evidence	Inferred From	Ref(s)
Biological Process	G-protein coupled receptor protein signaling	IDA		J:81728

Figure 3. GO annotations as text. In response to user requests, we have created a lexicon and templates that enable computational generation of GO annotations in text form. This is provided to our web interface users in conjunction with the tabular presentation of the GO annotation information. Here, the GO text for gene *Ednrb* annotations is presented.

HIGH LEVEL OVERVIEW OF THE MAIN COMPONENTS AND IMPLEMENTATION

The MGD database and software system was first released on the web in 1994. Here, we summarize the high level functionality of the major components of the system. At the heart of MGD is the database itself. MGD is implemented in the Sybase relational database management system. Its many tables form the core within which the biological information is stored. Additional sequence data such as BLAST-able databases and genome assembly files are stored outside the relational database. There are two primary vehicles by which data are entered into MGD: the editing interface and automated load programs. The editing interface (EI) is an interactive, graphical application. Curators use the EI to enter new data from the literature, to verify the results of automated loads and to correct errors. The automated load programs integrate larger datasets from many sources into the database. Automated loads involve 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. Through these two vehicles, the EI and automated loads, we are able to acquire and integrate large amounts of data into high-quality, curated information.

There are several different routes for public data access. The web interface (WI) is the main tool allowing users to query interactively and display our data through a web browser. MouseBLAST allows users to do sequence similarity searches against a variety of rodent-relevant sequence databases that are culled weekly from NCBI, UniProt and other providers. Mouse GBrowse (see above) allows users to visualize mouse datasets against the genome as a series of linear tracks. Supplementing these three interactive tools is a large collection of public database reports generated nightly. These reports provide concise listings of large subsets of data, for example, all mouse/human homologies. They 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. Direct SQL access to the database is available for sophisticated users who wish to construct custom queries or to perform analyses not possible through the WI. Finally, we have an initial web services API that is providing programmatic access to MGD. This API is designed for specific groups outside of MGI that access our data. A more robust and general API is planned for the near future.

CITING MGD

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.). For general citation of the Mouse Genome Informatics (MGI) resource please cite this article.

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Conflict of interest statement. None declared.

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