The Mouse Genome Database (MGD): integrating biology with the genome

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ABSTRACT

The Mouse Genome Database (MGD) is one component of the Mouse Genome Informatics (MGI) system (http://www.informatics.jax.org), a community database resource for the laboratory mouse. MGD strives to provide a comprehensive knowledgebase about the mouse with experiments and data annotated from both literature and online sources. MGD curates and presents consensus and experimental data representations of genetic, genotype (sequence) and phenotype information including highly detailed reports about genes and gene products. Primary foci of integration are through representations of relationships between genes, sequences and phenotypes. MGD collaborates with other bioinformatics groups to curate a definitive set of information about the laboratory mouse and to build and implement the data and semantic standards that are essential for comparative genome analysis. Recent developments in MGD discussed here include an extensive integration of the mouse sequence data and substantial revisions in the presentation, query and visualization of sequence data.

INTRODUCTION

The Mouse Genome Database (MGD) provides an integrated view of genetic and genomic information for the laboratory mouse (1,2). MGD contains information on mouse genes, genetic markers and genomic features as well as the associations of these features with molecular segments (i.e. probes, primers, cDNA clones, BACs and YACs) and mutant phenotypes. The database also includes comparative mapping data, graphical displays of linkage, cytogenetic and physical maps, experimental mapping data, as well as strain distribution patterns for recombinant inbred strains (RIs), recombinant congenic strains (RCs) and cross haplotypes. MGD is updated daily. A recent snapshot of MGD content is shown in Table 1. Since it first became available on the WWW, MGD has continued to evolve, expanding its data coverage, improving data handling and providing several new data manipulation and display tools.

MGD is one component of the Mouse Genome Informatics (MGI) database resource (http://www.informatics.jax.org) located at the Jackson Laboratory (http://www.jax.org). Other projects and resources that contribute to MGI include the Gene Expression Database (GXD) (3), the Mouse Genome Sequencing (MGS) project and the Mouse Tumor Biology Database (MTB; http://tumor.informatics.jax.org/). The MGI consortium group participates actively in the development and implementation of the Gene Ontologies (GOs) (http://www.geneontology.org). MGI curators also collaborate extensively with Swiss-Prot, RIKEN, and with the LocusLink project at the NCBI to evaluate associations between genes and sequences for the mouse.

IMPROVEMENTS DURING 2003

Integration of sequence data into MGI

A major advance in data representation and integration in the MGI system developed during this year has been to fully integrate mouse sequence and sequence feature annotations. Prior to the integration of sequence data into the database, MGD curators documented the association of sequence data with genes, probes and markers on the basis of curated annotations of literature and/or data loads (e.g. through shared curation of sequence links between MGI and Swiss-Prot, NCBI LocusLink and RIKEN). The connection between sequences and biological entities in the database were represented in MGD only as a table of associations between accession identifiers. Hypertext links were provided from the MGD Gene Detail Pages to the sequence data in GenBank/EMBL/DDBJ and Swiss-Prot. The MouseBLAST (http://mouseblast.informatics.jax.org) server, which is maintained by the MGI consortium, provided a mechanism to query the database using nucleotide or protein sequences. Until recently however, sequence data per se were not stored in the MGI database system and users could not query the database using such sequence attributes as strain, sequence type, sequence length, etc. The new enhancements in sequence representation

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in the MGI system include the incorporation of all available sequence data for the mouse into MGI, the normalization of sequence feature annotations from NCBI and from providers of large cDNA sequence sets, and the development of query and visualization components specific to sequence representations.

The sequence data that have been and are being integrated into the MGI database system include the RIKEN full-length cDNA clone data sets (4), the Mammalian Gene Collection (MGC) clone data (5), computational gene models from Ensembl and the NCBI's annotation of the reference mouse genome sequence (6), and ‘virtual’ transcript data sets from The Institute for Genomic Research (TIGR Mouse Gene Index) and the Computational Biology and Informatics Laboratory (CBIL) at the University of Pennsylvania (7). Sequence and clone information for such commonly used clone libraries as the National Institute on Ageing (NIA) set and the RPCI-23 and -24 BAC clones have also been incorporated into the database. For each sequence set, a combination of manual and computational approaches for sequence to gene correlations assured the correct data associations [see (7–9) for detailed descriptions of sequence annotation processes]. Each sequence–gene association is documented independently so that modifications in the gene–sequence sets can be facilitated. MGI curation staff normalized sequence feature annotations including (i) strain names, (ii) library name, (iii) type of sequence and (iv) tissue of origin. Sequence features represented in MGI include these four attributes as well as sequence length, reference of origin and clone collection (if applicable). As a result, users can submit complex queries based on sequence attributes and filtered by other gene-specific information such as functional attributes or time/tissue of expression (Fig. 1). Sequence summary reports (Fig. 2) and sequence detail reports (Fig. 3) incorporate detailed information about the sequence. It is now possible for users of the MGI system to download sequence data directly from the database instead of having to follow a series of hypertext links before they can access the actual sequences associated with a gene or other marker in MGD.

### Enhanced queries by gene

A new feature on the ‘Genes and Markers Query Form’ provides an improved option for gene name text searches. Whereas previous nomenclature queries examined current symbols/names and synonyms, the new default query also searches the allele symbols/names and human gene symbols/names. The summary results present a list of matches on the query term ordered by matches on the current symbol, current name, allele symbol, allele name, withdrawn symbol, withdrawn name, synonym, human ortholog symbol, human ortholog name and all other ortholog symbols. Each item of information is linked to a detail page. If the information being sought is not present on the list, it is possible to determine, at a glance, how to narrow the query by altering the search string.

### Enhanced gene detail reports

Two major enhancements of the gene detail page include the presentation of short statements about the phenotype(s) associated with the gene, and a new presentation of summary information about the sequence of the gene (Fig. 4). The short phenotype descriptions are tied to the manual curation of model mutant and allele phenotype data and thus will be reviewed each time new mutant phenotype data is annotated for the gene. The summary sequence data expands the representation of map position to include the sequence coordinates (currently from the EnsEMBL annotation of NCBI Build 30) and a link to the EnsEMBL ContigView and to the UCSC Browser. The incorporation of links from MGI to the MapViewer at NCBI are planned.

### OTHER INFORMATION

#### User input

MGD encourages user input into its gene and allele annotation efforts. On each gene detail and allele detail page, a clickable button (‘Your Input Welcome’) brings the user to a web-based form for submitting updates to the information being viewed.

#### 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 mouse (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. Scientists can reserve symbols prior to publication using the electronic nomenclature submission form (http://www.informatics.jax.org/mgihome/nomen/nomen_submit_form.shtml) or by contacting the MGD nomenclature coordinator by email (nomen@informatics.jax.org). The MGD nomenclature coordinator can also assist with other nomenclature issues such as revision of gene family designations.

Electronic data submission

Any type of data that MGD maintains can be submitted as an electronic contribution, although mapping data, polymorphisms and mammalian homologies are currently the most common. Each electronic submission receives a permanent database accession ID. All data sets are associated with either an electronic submission reference or a published paper. MGD reference pages provide links to associated data sets. Online information about data submissions procedures is found at http://www.informatics.jax.org/mgihome/.
Figure 2. Sequence Summary Report. The expanded Sequence Summary Report displays the query summary at the top of the page, and provides details about the sequences returned by the query including the type, length, strain and description. In addition to links to a Sequence Detail Report, sequences can be selected and either downloaded in FASTA format or forwarded to MouseBLAST. This Summary Report shows the results from the query described in Figure 1 and shows a mRNA for each of the five genes that matched the query criteria. These genes are \textit{Cd28}, \textit{Ctla4}, \textit{Icos}, \textit{Ccl20} and \textit{Il10}.

Figure 3. Sequence Detail report. The new Sequence Detail report for the RefSeq record, NM_009843, shows the sequence attributes, source attributes, and the genes that have been annotated to this sequence. A summary of additional data curated for the gene is displayed with links to the detail reports for those data.
Community outreach and user support

MGD provides extensive user support through online 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. Other outreach includes online tutorials and answers to frequently asked questions, available at http://www.informatics.jax.org/userdocs/helpdocs_menu.shtml. Lee Silver’s book, Mouse Genetics, is now available in an electronic version at http://www.informatics.jax.org/silver/. The online version has been enhanced by linking genes and references to MGI and MEDLINE.

IMPLEMENTATION

MGD is implemented in the Sybase relational database system, version 12.5. A large set of CGI scripts and Java Servlets mediates the user’s interaction with the database. For computational users, direct SQL access can be requested through User Support. User-requested database reports and a number of widely used data files (generated daily) are available on the FTP site (ftp://ftp.informatics.jax.org).

CITING MGD

The following citation format is suggested when referring to data sets 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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REFERENCES


