7. Online Mendelian Inheritance in Man (OMIM): A Directory of Human Genes and Genetic Disorders

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Summary

Online Mendelian Inheritance in Man (OMIM [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM]TM*) is a timely, authoritative compendium of bibliographic material and observations on inherited disorders and human genes. It is the continuously updated electronic version of *Mendelian Inheritance in Man* (MIM). MIM was last published in 1998 (1) and is authored and edited by Dr. Victor A. McKusick and a team of science writers, editors, scientists, and physicians at The Johns Hopkins University [http://www.jhu.edu] and around the world (2). Curation of the database and editorial decisions take place at The Johns Hopkins University School of Medicine. OMIM provides authoritative free text overviews of genetic disorders and gene loci that can be used by clinicians, researchers, students, and educators. In addition, OMIM has many rich connections to relevant primary data resources such as bibliographic, sequence, and map information.

Content and Access

OMIM Entries

OMIM [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM] comprises descriptive, full-text MIM entries, a tabular Synopsis of the (Human Gene Map [http://www.ncbi.nlm.nih.gov:80/htbin-post/Omim/getmap]) that includes the Morbid Map [http://www.ncbi.nlm.nih.gov:80/htbin-post/Omim/getmorbid], clinical synopses, and mini-MIMs.

OMIM entries are authored and edited by experts in the field and by the OMIM staff, based on information in the published literature. All entries are assigned a unique, stable, six-digit ID number and provide names and symbols used for the disorder and/or gene, a literature-based description, citations, contributor information, and creation and editing dates. Because MIM is derived from the primary literature, the text is replete with citations and links to PubMed. OMIM authors create entries for each unique gene or Mendelian disorder for which sufficient information exists and do not wittingly create more than one entry for each gene locus.

MIM is organized into autosomal, X-linked, Y-linked, and mitochondrial catalogs, and MIM numbers are assigned sequentially within each catalog (Table 1). The kinds of information that may be included in MIM entries are approved name and symbol (obtained from the HUGO Nomenclature Committee), alternative names and symbols in

common use, and a text description of the disease or gene. Many of the longest entries and most new entries in MIM have headings within the text that may include Clinical Features, Inheritance, Population Genetics, Heterogeneity, Genotype/Phenotype Correlations, Cloning, Gene Structure, Gene Function, Mapping, and more. Information on selected disease-causing mutations is contained in the Allelic Variant section of the entry describing the gene.

Table 1. The OMIM numbering system.

MIM number range[a]	Explanation
100000-199999	Autosomal loci or phenotypes (entries created before May 15, 1994)
200000-299999	Autosomal loci or phenotypes (entries created before May 15, 1994)
300000-399999	X-linked loci or phenotypes
400000-499999	Y-linked loci or phenotypes
500000-599999	Mitochondrial loci or phenotypes
600000-	Autosomal loci or phenotypes (entries created after May 15, 1994)

[a] MIM numbers are frequently preceded by a symbol. An asterisk (*) before a MIM number indicates that the entry describes a distinct gene or phenotype and that the mode of inheritance of the phenotype has been proved (in the judgment of the authors and editors) and that the phenotype described is not known to be determined by a gene represented by other asterisked entries in MIM. A number sign (#) before a MIM number describing a phenotype indicates that the phenotype is caused by mutation in a gene represented by another entry and usually in any of two or more genes represented by other entries. The number sign is also used for phenotypes that result from specific chromosomal aberrations, such as Down syndrome, and for contiguous gene syndromes, such as Langer-Giedion syndrome. Whenever a number sign is used, the reason is stated at the outset of the entry.The absence of an asterisk (or other sign) preceding the number indicates that the distinctness of the phenotype as a mendelizing entity or the characterization of the gene in the human is not established.

With the increasing complexity of biological information, OMIM makes a critical contribution by distilling what is known about a gene or disease into a single, searchable entry. The rich text of the OMIM entry, along with the source reference citations, make it easy to retrieve data of interest. The OMIM entry can then serve as a gateway to other sources of related information via the many curated and computed links within each entry.

The OMIM Gene Map

The OMIM Synopsis of the Human Gene Map [http://www.ncbi.nlm.nih.gov:80/htbin-post/Omim/getmap] is a tabular listing of the genes and loci represented in MIM ordered pter to qter from chromosome 1–22, X, and Y. The information in the map includes the cytogenetic location, symbol, title, MIM number, method of mapping, comments, associated disorders and their MIM numbers, and the map location of the mouse ortholog. Links are provided from the cytogenetic location to the human Map Viewer [http://www.ncbi.nlm.nih.gov/mapview], from MIM numbers to OMIM entries, and from mouse map locations to the Mouse Genome Database (MGD [http://www.informatics.jax.org/]).

The Synopsis of the human gene map has also been sorted alphabetically by disorder and is referred to as the Morbid Map.

Access

OMIM can be found either by direct query via Entrez [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM], from other data resources within NCBI that connect to OMIM directly (for example, LocusLink or UniGene), or through Entrez cross-indexing (for example, from a PubMed abstract of an article cited in an OMIM entry). OMIM is indexed for retrieval in Entrez using a weighted system so that if the query term(s) appears in the title of a MIM entry, it will appear at the top of the retrieval list. Field restrictions [http://www.ncbi.nlm.nih.gov/entrez/Omim/omimhelp.html#SearchFields]

are supported for some types of information, or one can use the **Limits** page to restrict a search (Figure 1). There are also several format options for viewing a retrieval set that may affect which entries are displayed (Box 1).

Figure 1: The Limits options for searching OMIM in Entrez.

Queries can also be entered in the query box shown on all Entrez database pages, selecting OMIM as the database in the **Search** option. The **Preview/Index,History, Clipboard**, or Cubby functions can also be used for OMIM, as for the rest of Entrez.

The Gene Map can be accessed from an individual OMIM entry via the cytogenetic location displayed when appropriate under the entry titles. The Gene Map may also be queried directly [http://www.ncbi.nlm.nih.gov/htbin-post/Omim/getmap]. When queried directly, the first entry that matches the query is shown in the top row of the table, followed by 19 entries ordered by cytogenetic location. The **Find Next** button can be used to find additional gene map entries that match the query.

Guide to OMIM Pages

Query Bar

OMIM is queried via a standard Entrez query bar. The mechanics of selecting entries to display, how to display them, and identifying related entries either within Entrez or from external resources is also according to the Entrez/LinkOut standard. The display options (Box 1) allow the user to format results in several ways. A useful function particular to OMIM is the option to display **Allelic Variants**, **Clinical Synopsis**, or **mini-MIM** views for a retrieval set.

OMIM Navigation

The OMIM homepage [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM] and the search results pages share the same navigational links to the advanced query [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM&cmd=Limits] page (Gene Map [http://www.ncbi.nlm.nih.gov/htbin-post/Omim/getmap], Morbid Map [http://www.ncbi.nlm.nih.gov/htbin-post/Omim/getmorbid]), Help [http://www.ncbi.nlm.nih.gov/entrez/Omim/omimhelp.html] documents, FAQs [http://www.ncbi.nlm.nih.gov/entrez/Omim/omimfaq.html], statistics [http://www.ncbi.nlm.nih.gov/entrez/Omim/dispupdates.html], and related resources [http://www.ncbi.nlm.nih.gov/entrez/Omim/allresources.html].

When viewing the text of an OMIM entry, however, the navigational links serve as an electronic table of contents. The section headings within the entry are listed similar to a table of contents, and selecting one moves the display to that section. Within an entry, selecting the `MIM #` link takes you back to the top of the entry.

OMIM staff actively contributes to the curation of data in LocusLink. Thus, if the MIM number is represented in LocusLink, a reciprocal LocusLink link is provided in the section to the left. Other links provided by the LocusLink collaboration may also be listed in this section, e.g., links to Nomenclature, Reference Sequences, or UniGene clusters that are specific to the subject OMIM entry.

The sequence links in the LocusLink section may be different from the Entrez indexing links available via the `Links` link at the top right of an entry. The Entrez indexing links result indirectly from the references in the OMIM entry and may include related sequences in other species, for example. Thus, OMIM pages allow two levels of sequence connection: the specific ones in the left section under LocusLink and the indirect but still informative ones through Entrez indexing link at the upper right. More information on OMIM link types can be found in the Help [http://www.ncbi.nlm.nih.gov:80/entrez/ Omim/omimhelp.html#LinkTypesOverview] documents.

OMIM entries may also contain a link to LinkOut for resources external to NCBI (see Chapter 16). Some of these external resouces are curated by OMIM staff, in which case they are displayed by name. Others can be seen either by selecting `LinkOut` in the `Links` pull-down menu or by selecting the `LinkOut` display option in the query bar.

Entrez Links

At the top of any report page, or associated with each entry in the query result page, are the links to related data generated from Entrez (Chapter 14). Here, PubMed links to the PubMed abstracts of the reference citations in the entry. `Related Entries` are to all other OMIM entries referenced in the subject entry. `Nucleotide`, `Protein`, and `LinkOut` connections are as documented in the previous section.

The OMIM Entry

Each OMIM entry has a unique number and is given a primary title and symbol. This is the title that is displayed in the document retrieval list. Alternative designations are listed below the primary title. Some entries contain information that is related but not synonymous to the primary topic and is not addressed in another entry (e.g., splice variants, phenotypic variants, etc.). This information is set off by the word "included" in the title. The first "included" title is displayed in the document retrieval list. The cytogenetic map location when known is given for each entry. When a disease shows genetic heterogeneity, more than one map location may be given. The "light bulb" icon at the end of text paragraphs links to related articles in PubMed. References within the text are linked to the complete citation at the end of the entry. There, the PubMed ID is linked to the PubMed abstract.

Some entries contain an `Allelic Variants` section, which lists noteworthy mutations for the gene. Allelic variants are given a 10 digit number: the 6-digit number of the parent locus, followed by a decimal point and a unique 4-digit variant number. Criteria for inclusion include the first mutation to be discovered, high population frequency, distinctive phenotype, historic significance, unusual mechanism of mutation, unusual pathogenetic mechanism, and distinctive inheritance (e.g., dominant with some mutations, recessive with other mutations in the same gene). Most of the allelic variants represent disease-producing mutations. A few polymorphisms are included, many of which show a statistically significant association with specific common disorders.

FTP

The OMIM data are available for bulk transfer [http://www.ncbi.nlm.nih.gov/entrez/Omim/omimfaq.html#download], but it should be noted that there are **restrictions on use**.

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Legal Statement

OMIM is funded by a contract from the National Library of Medicine and the National Human Genome Research Institute and by licensing fees paid to the Johns Hopkins University by commercial entities for adaptations of the database. The terms of these licenses are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.

References

1. McKusick VA, et al. Mendelian Inheritance in Man. 12th ed. Baltimore: Johns Hopkins University Press; 1998.

2. Hamosh A. Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders. Nucleic Acids Res 30:52–55; 2002.

Box 1: Display options for viewing OMIM query results.

Title (default)

Details

Clinical Synopsis

Allelic Variants

mini-MIM

ASN.1

LinkOut

Related Entries

Genome Links

Nucleotide Links

Protein Links

PubMed Links

SNP Links

Structure Links

UniSTS Links

Obtaining multiple views of a query result:

1. Enter query term or terms (example: renal failure hypertension).

2. Default display is **Titles**.

3. Select **Clinical Synopsis** and click on **Display** at the left to see the **Clinical Synopsis** section of all entries that have them.

4. Similarly, select **mini-MIM** or **Allelic Variants**.

NOTE: In the same bar, the number of entries to display and the format in which to display them can be configured by use of the **Show** and **Text** buttons, respectively.