Mouse Genome Informatics www.informatics.jax.org
The fundamental mission of the Mouse Genome Informatics resource is to facilitate the use of mouse as a model system for understanding human biology and disease.

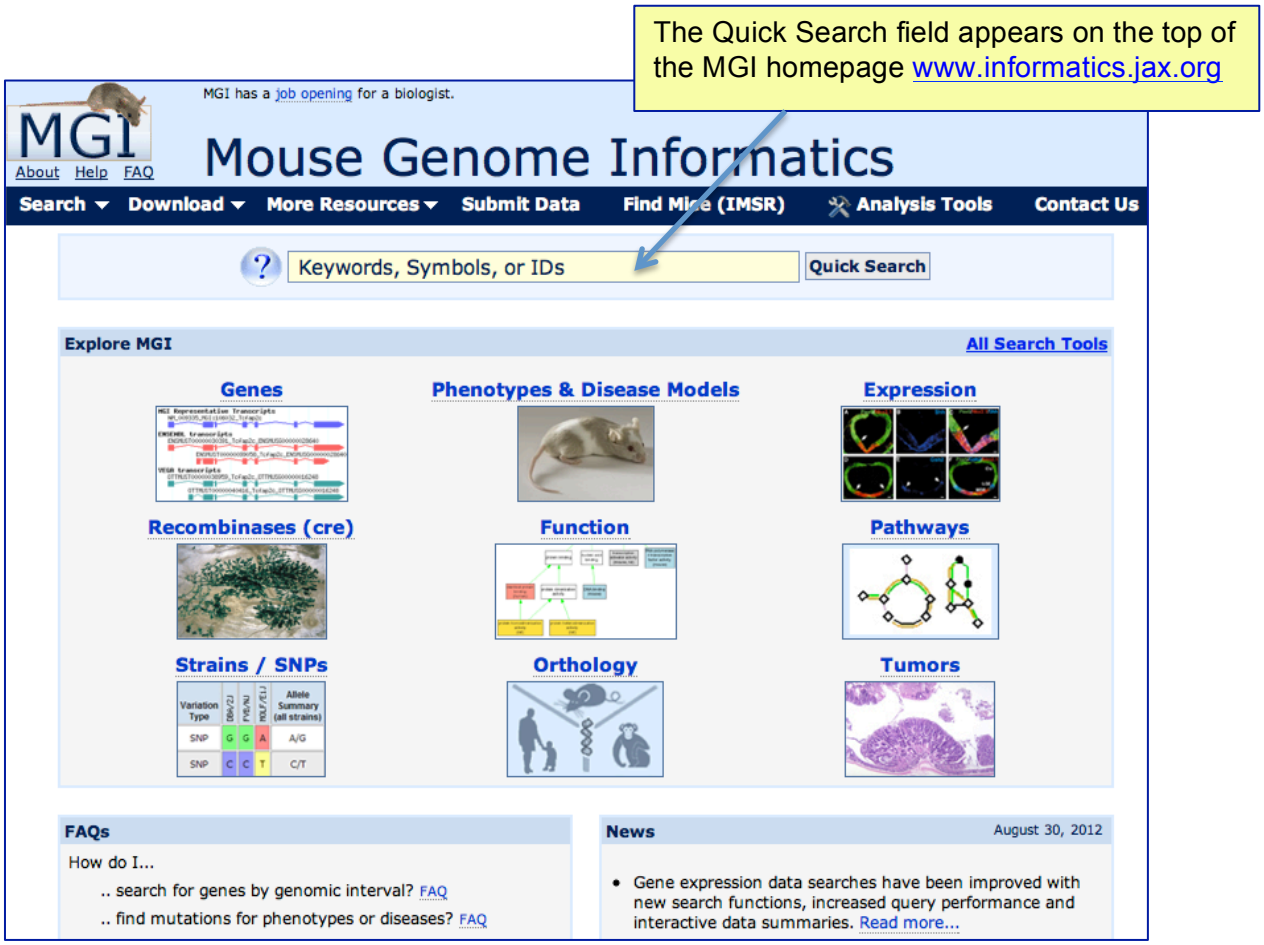
Human Disease Models Tutorial

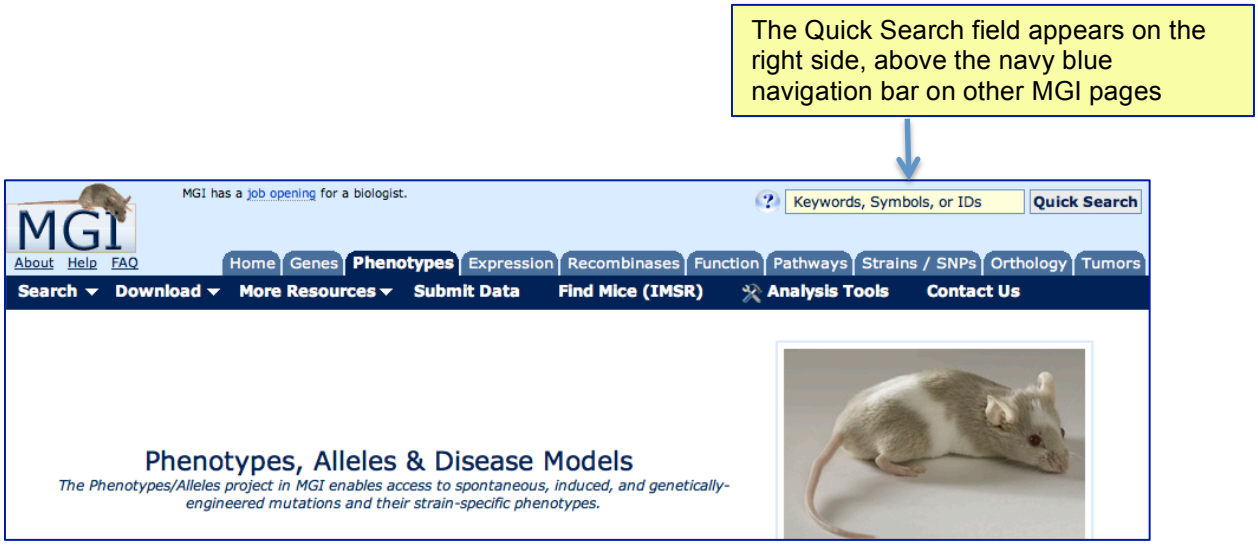
This tutorial will demonstrate some of the many ways to use MGI to:

- Find mouse models of human diseases
- Find mouse genotypes associated with specific phenotypes
- Find detailed phenotypic data associated with mouse alleles
- Find available mouse resources from repositories
- Obtain sets of relevant data for your own analyses

Contents

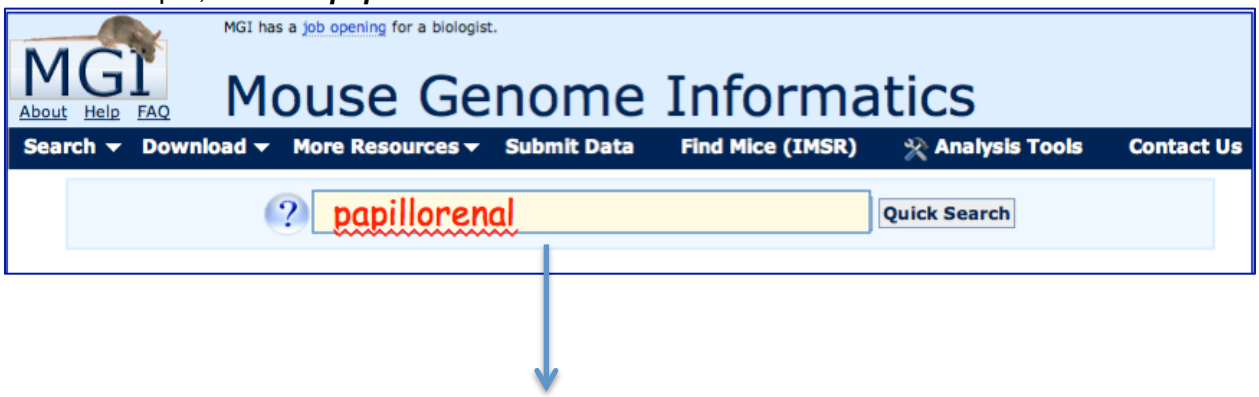
Using the Quick Search. A Quick Search field is available on almost all MGI web pages and allows you quickly to jump to a topic of interest.

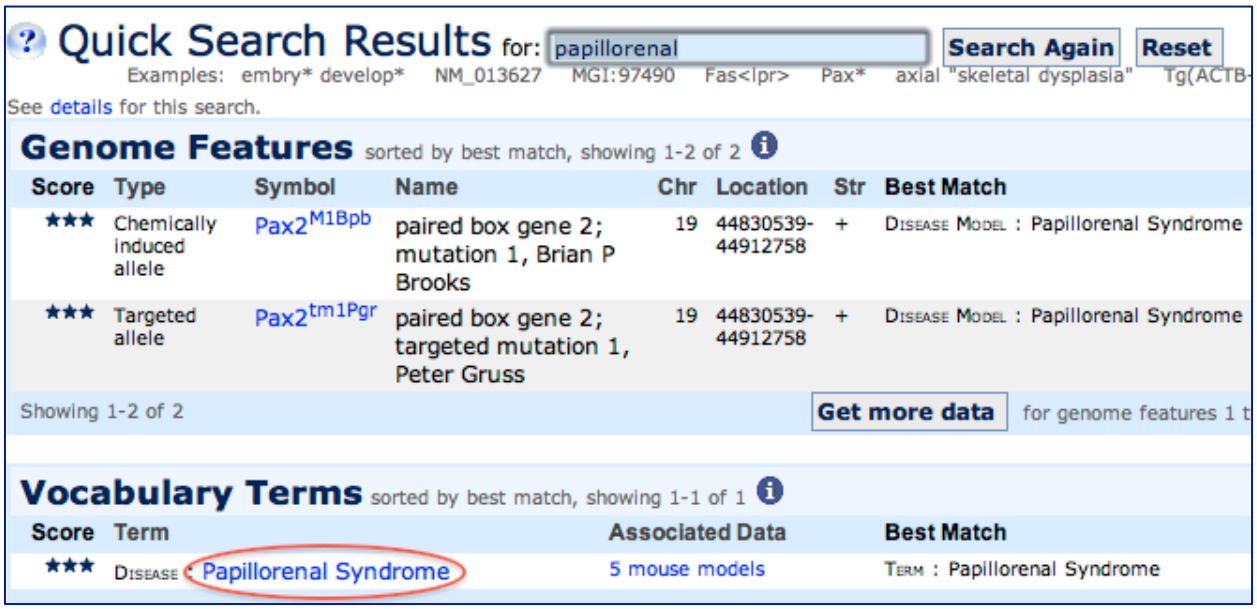




You can type *any alphanumeric string*, including **keywords** (genes, gene symbols, phenotypes, disease terms, etc.) or **accession identifiers** (from GenBank, NCBI, Ensembl, PubMed, MGI, etc.) into the Quick Search box.

In this example, the term ***papillorenal*** has been entered into the search field:





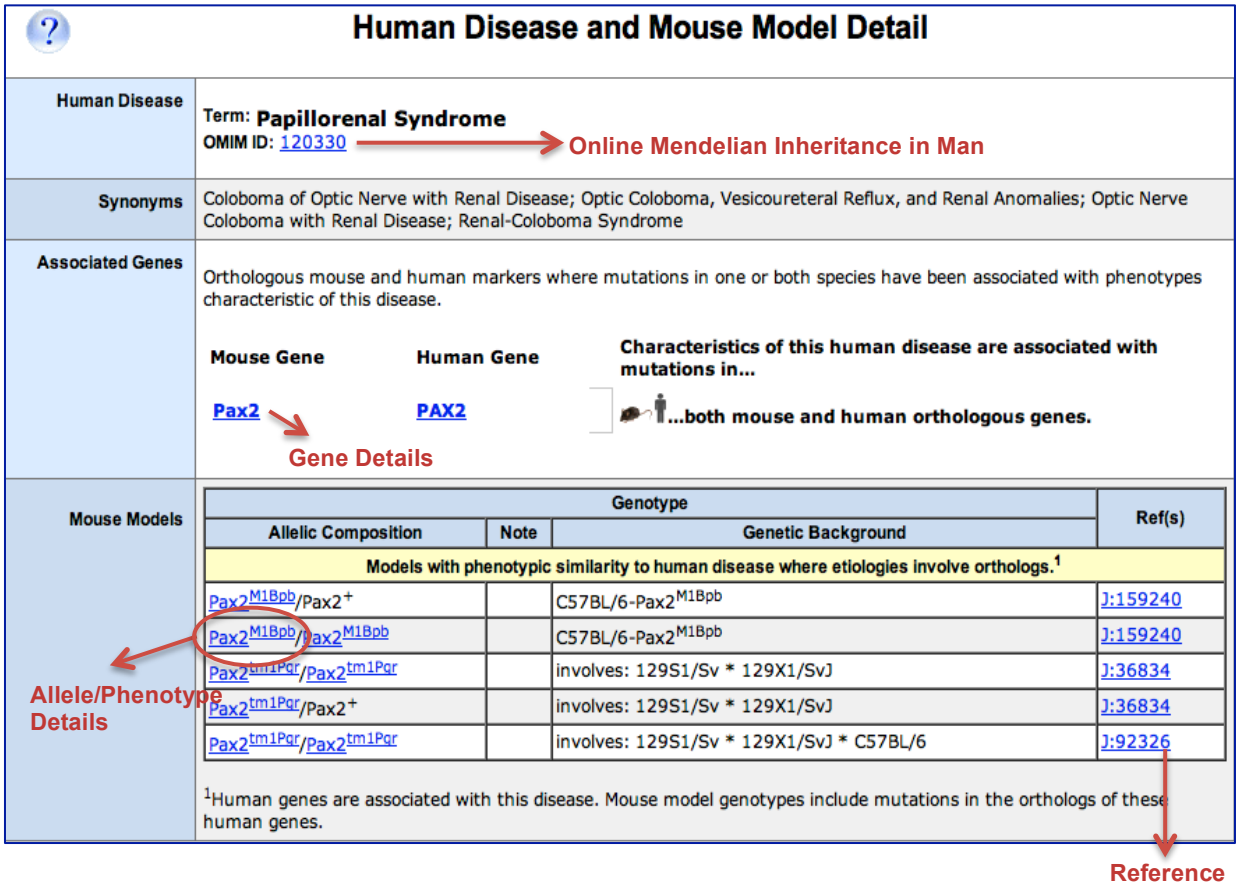
The Quick Search returns results in two sections:

Genome Features: matches found based on nomenclature for genes and mutations
Vocabulary Terms: matches based on diseases, phenotypes, or other keywords.

In the Genome Feature section, two mutant alleles, each annotated to the human disease term "Papillorenal Syndrome", have been found. The allele symbols (blue) link directly to allele detail pages (see page 5) of this tutorial.

In the Vocabulary Term section, the disease term "Papilloreanal Syndrome" has been found with 5 mouse models associated. Clicking on the disease term, will lead you to the Human Disease and Mouse Model Detail page for Papillorenal Syndrome.

Understanding the Human Disease and Mouse Model Detail page



The Human Disease and Mouse Model Detail page provides, for the given disease,

Human Disease Name: the OMIM (Online Mendelian Inheritance in Man) disease term and a link to the OMIM record.

Associated Genes: genes in *mouse and human* associated with this disease.

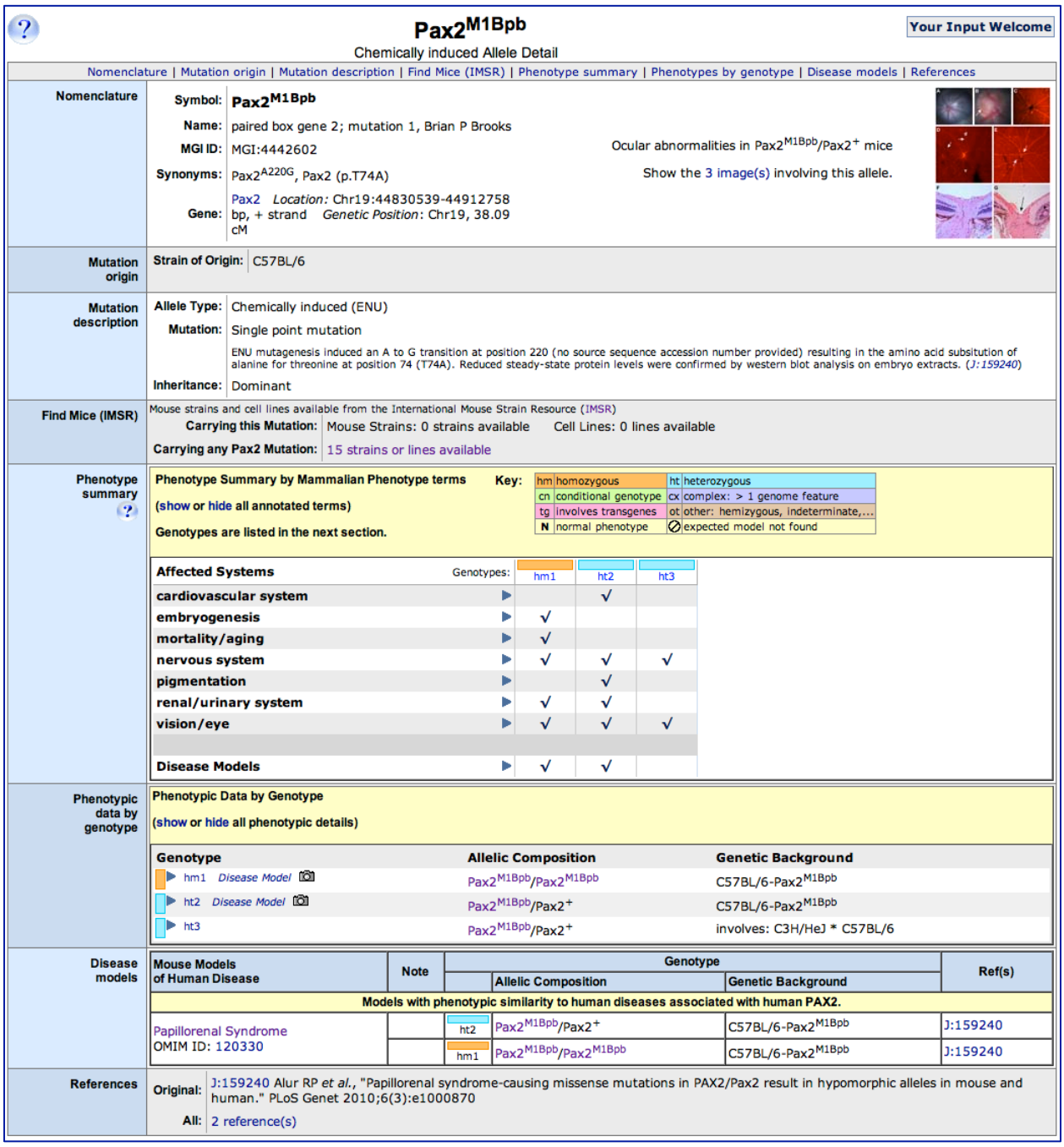
Mouse Models: mouse genotypes published as human disease models; with links to the corresponding detail pages for the allele / phenotype data and to supporting references.

Under the Mouse Model Section of this page, the 5 unique mouse model genotypes are specified.

The following page shows a detail page for the mutant allele *Pax2*^{M1Bpb}, the first mutation (M1) in the *Pax2* gene, developed in the laboratory of Brian P Brooks (Bpb).

(note that this same detail page for *Pax2*^{M1Bpb} could have been accessed alternatively from links on the Quick Search results shown on page 3 of this tutorial) .

Allele/Phenotype Detail page for *Pax2^{M1Bpb}*



Pax2^{M1Bpb}

Chemically induced Allele Detail

Your Input Welcome

Nomenclature | Mutation origin | Mutation description | Find Mice (IMSR) | Phenotype summary | Phenotypes by genotype | Disease models | References

Nomenclature

Symbol: Pax2^{M1Bpb}
Name: paired box gene 2; mutation 1, Brian P Brooks
MGI ID: MGI:4442602
Synonyms: Pax2^{A220G}, Pax2 (p.T74A)
Gene: Pax2 *Location:* Chr19:44830539-44912758 bp, + strand *Genetic Position*: Chr19, 38.09 cM

Ocular abnormalities in Pax2^{M1Bpb}/Pax2^{+} mice
Show the 3 image(s) involving this allele.

Mutation origin

Strain of Origin: C57BL/6

Mutation description

Allele Type: Chemically induced (ENU)
Mutation: Single point mutation
ENU mutagenesis induced an A to G transition at position 220 (no source sequence accession number provided) resulting in the amino acid subsitution of alanine for threonine at position 74 (T74A). Reduced steady-state protein levels were confirmed by western blot analysis on embryo extracts. (*J:159240*)
Inheritance: Dominant

Find Mice (IMSR)

Mouse strains and cell lines available from the International Mouse Strain Resource (IMSR)
Carrying this Mutation: Mouse Strains: 0 strains available Cell Lines: 0 lines available
Carrying any Pax2 Mutation: 15 strains or lines available

Phenotype summary

Phenotype Summary by Mammalian Phenotype terms
(show or hide all annotated terms)
Genotypes are listed in the next section.

Key: hm homozygous; ht heterozygous; cn conditional genotype; cx complex: > 1 genome feature; tg involves transgenes; ot other: hemizygous, indeterminate,...; N normal phenotype; ⊘ expected model not found

Affected Systems	Genotypes:	hm1	ht2	ht3
cardiovascular system			√	
embryogenesis		√		
mortality/aging		√		
nervous system		√	√	√
pigmentation			√	
renal/urinary system		√	√	
vision/eye		√	√	√
Disease Models		√	√	

Phenotypic data by genotype

Phenotypic Data by Genotype
(show or hide all phenotypic details)

Genotype	Allelic Composition	Genetic Background
hm1 *Disease Model*	Pax2^{M1Bpb}/Pax2^{M1Bpb}	C57BL/6-Pax2^{M1Bpb}
ht2 *Disease Model*	Pax2^{M1Bpb}/Pax2^{+}	C57BL/6-Pax2^{M1Bpb}
ht3	Pax2^{M1Bpb}/Pax2^{+}	involves: C3H/HeJ * C57BL/6

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 PAX2.					
Papillorenal Syndrome OMIM ID: 120330		ht2	Pax2^{M1Bpb}/Pax2^{+}	C57BL/6-Pax2^{M1Bpb}	J:159240
		hm1	Pax2^{M1Bpb}/Pax2^{M1Bpb}	C57BL/6-Pax2^{M1Bpb}	J:159240

References

Original: J:159240 Alur RP *et al.*, "Papillorenal syndrome-causing missense mutations in PAX2/Pax2 result in hypomorphic alleles in mouse and human." PLoS Genet 2010;6(3):e1000870
All: 2 reference(s)

1

2

This page contains many types of details, including characteristics of the molecular mutation, how to obtain mice carrying this mutation, specific phenotypes (expandable table, see pages 7-8 of this tutorial), images, disease models and references.

Here we look at two specific parts of this page: (1) finding mice with this mutation available from a repository and (2) examining details of the phenotypes.

(1) Finding available mice carrying *Pax2* mutations.

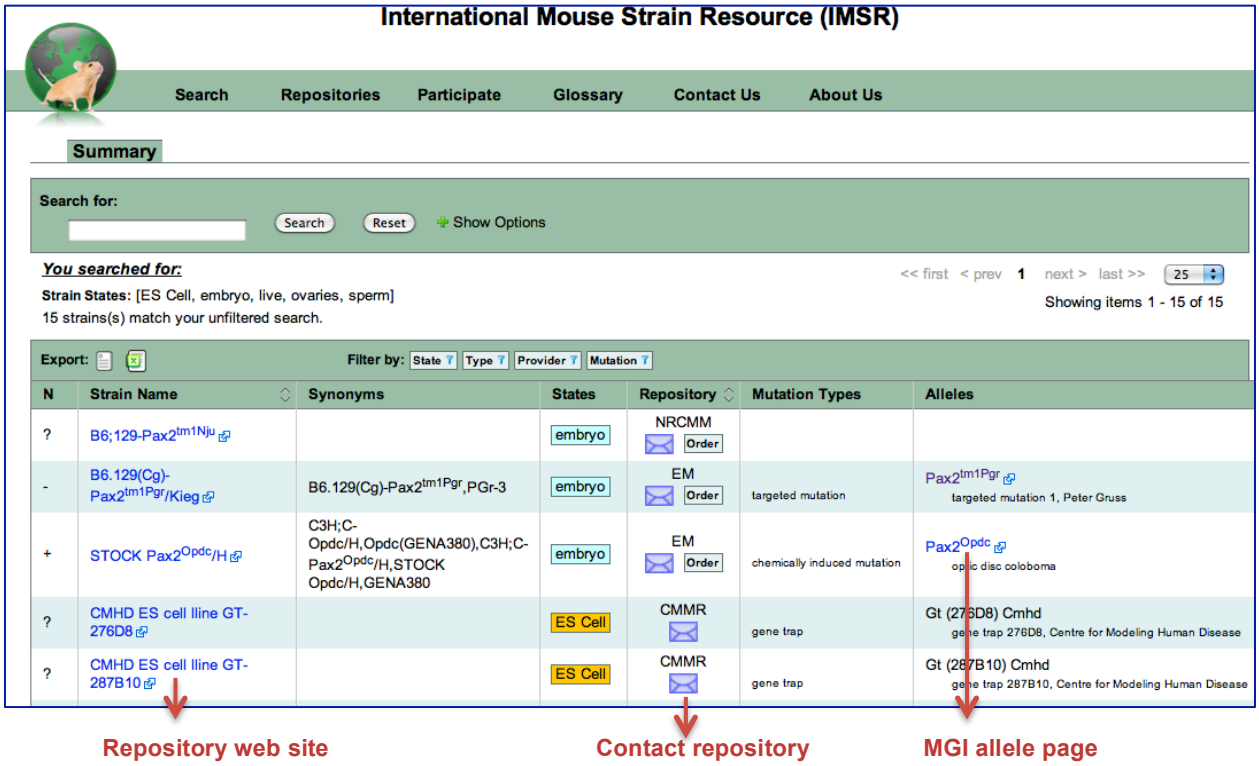
Find Mice (IMSR)	Mouse strains and cell lines available from the International Mouse Strain Resource (IMSR)
	Carrying this Mutation: Mouse Strains: 0 strains available Cell Lines: 0 lines available
	Carrying any Pax2 Mutation: 15 strains or lines available

Examine this portion of the Detail page shown on page 5 (labeled "1").
This tells us that

1) No mouse strains or cell lines from this particular *Pax2* mutation (*Pax2*^{M1Bpb}) are available from public repositories (but may be available from one of the publishing authors).
2) There are 15 strains of mice available carrying other mutations in the *Pax2* gene.

Clicking on the *15 strains or lines available* link will launch a search of the International Mouse Strain Resource (IMSR) for relevant strains from publicly available mouse repositories worldwide.

In the IMSR search results, shown below, items in the Strain Name column link to the repository's web site, the Repository column links to an e-mail or order form so you can request mice or ask about the stock and the Allele Symbol links to the MGI Allele Detail page like the one shown on page 5 of this tutorial.

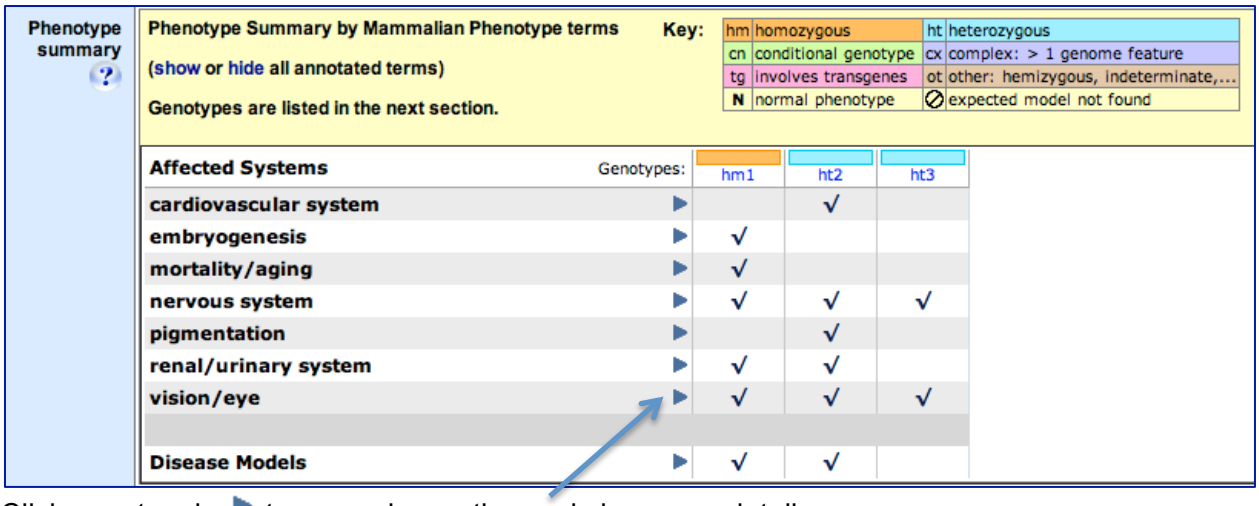


The International Mouse Strain Resource (IMSR) also can be searched directly for mouse strains of interest at http://www.findmice.org/.

Details of the Phenotypes

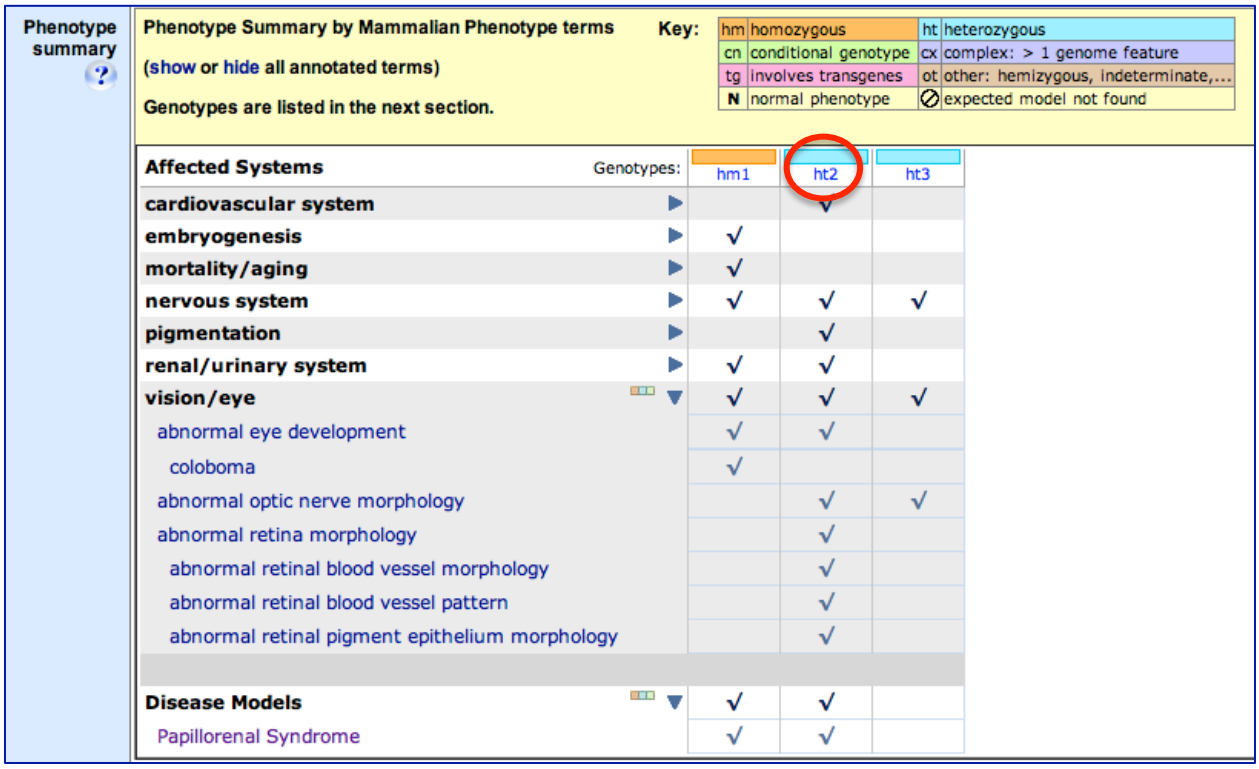
Moving to (2) examining details of the phenotypes section of the Allele Detail Page (see page 5 of this tutorial). If you are following these examples on your computer and wish to return directly to the Allele Detail page for *Pax2*^{M1Bpb}, go to:http://www.informatics.jax.org/accession/MGI:4442602.

The Phenotype summary section of the Allele Detail page shows a high-level view of the systems affected in mice carrying this mutation.

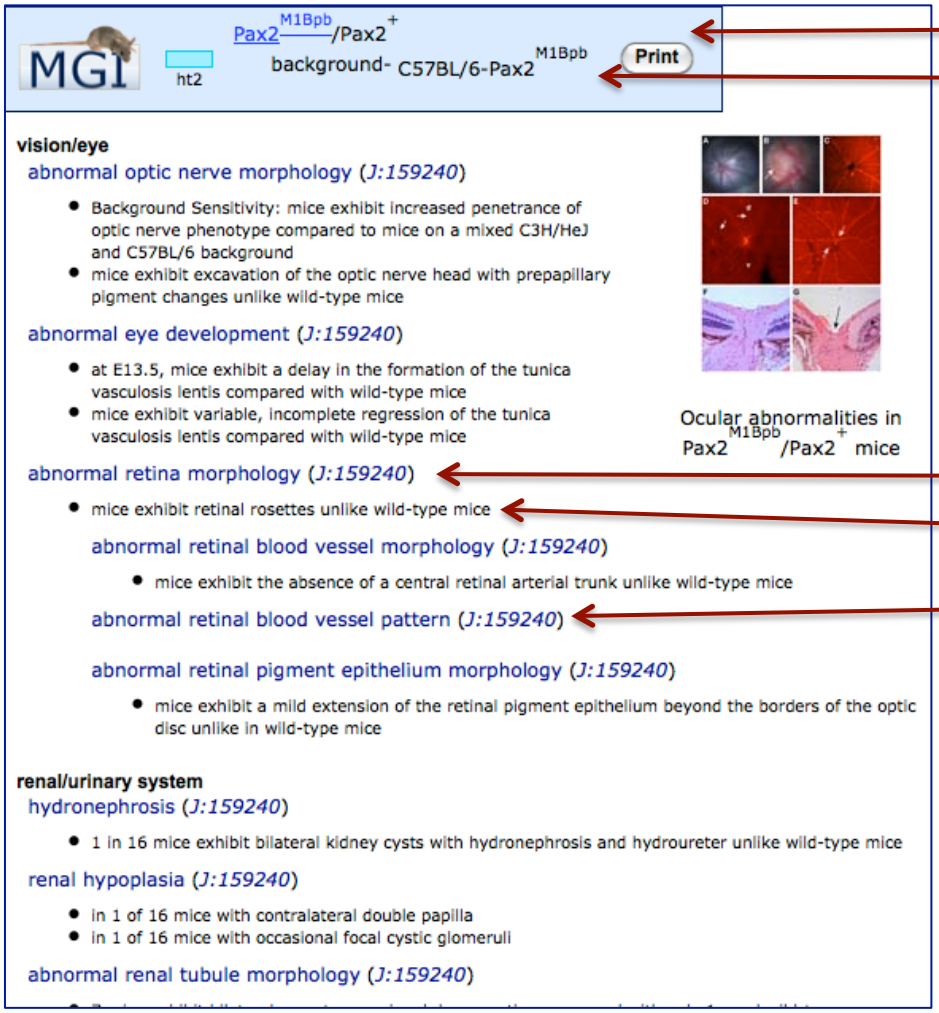


Click on a toggle ▶ to expand a section and view more details.

A portion showing the expanded *vision/eye* section is shown below. The Disease Models section has also been toggled and shows that this allele is a model for Papillorenal Syndrome.



In this grid view, a √ indicates the phenotype was detected. Each column represents a specific genotype, a combination of alleles and strain background. For details on the phenotypes shown for a specific genotype, click on an abbreviation, such as ht2 (heterozygous genotype #2). This launches a new browser window, a portion of which is shown below.



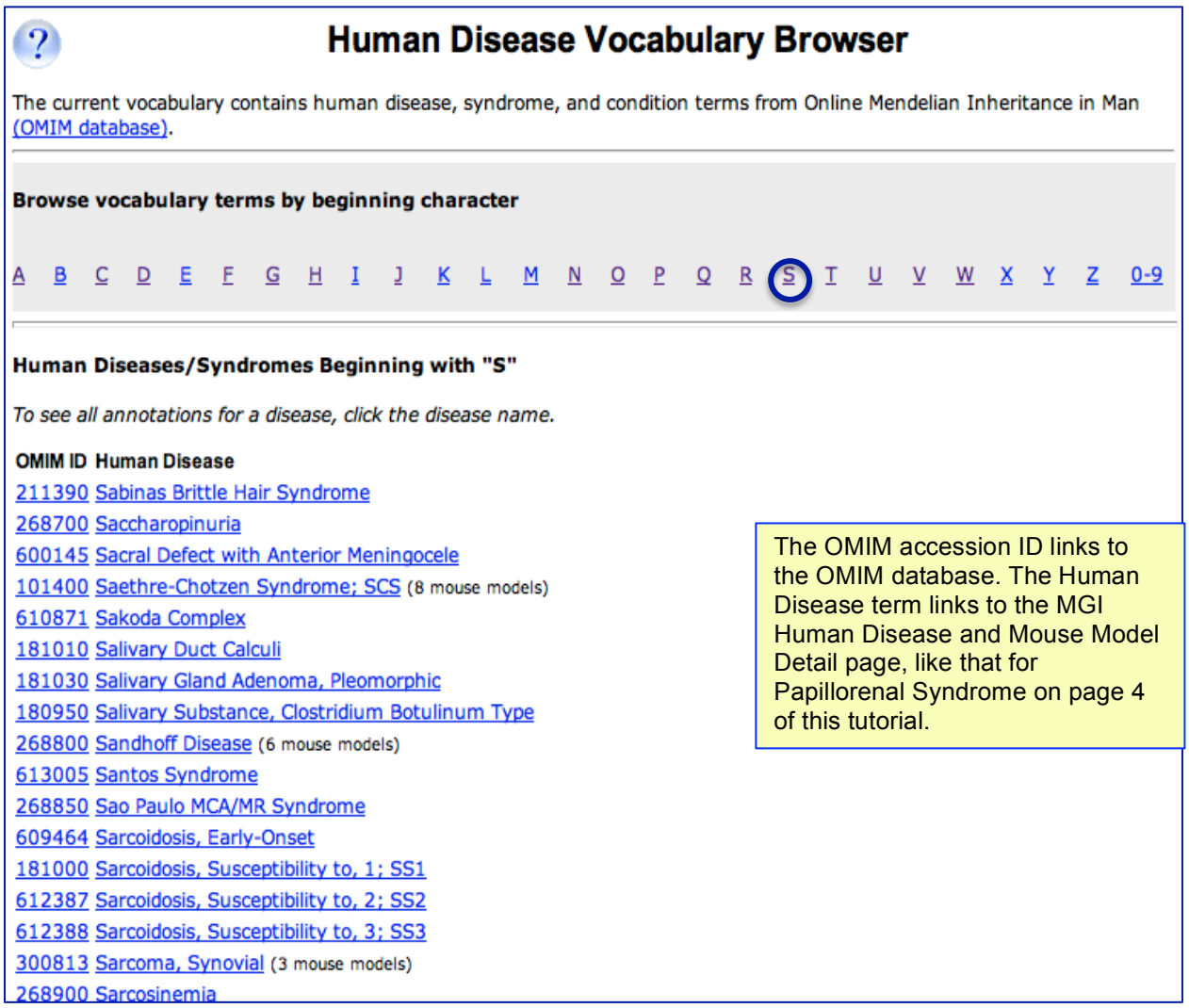
Browsing for Human Diseases

We started this tutorial by searching for a human disease using the MGI Quick Search tool and drilling down for additional information based on that first search.

Another way to find human disease, syndrome and condition terms derived from the Online Mendelian Inheritance in Man (OMIM) database is to browse Human Diseases. To do this, return to the *Pax2*^{M1Bpb} Allele Detail page (http://www.informatics.jax.org/accession/MGI:4442602), or use any MGI page and use the "Search" pull-down menu in the navy blue navigation bar along the top.

Using the **Search** drop down, select "Vocabularies" and then "Human Disease (OMIM)"

Within the Human Disease Vocabulary Browser, click any letter of the alphabet and a list of all OMIM diseases or syndromes beginning with that letter appears, arranged alphabetically (here showing the top portion of a browser page for diseases beginning with letter “S”). The number of mouse models in MGI appears in parentheses next to some disease names. The absence of this text means that MGI currently contains no mouse models for the disease.



Human Disease Vocabulary Browser

The current vocabulary contains human disease, syndrome, and condition terms from Online Mendelian Inheritance in Man (OMIM database).

Browse vocabulary terms by beginning character

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z 0-9

Human Diseases/Syndromes Beginning with "S"

To see all annotations for a disease, click the disease name.

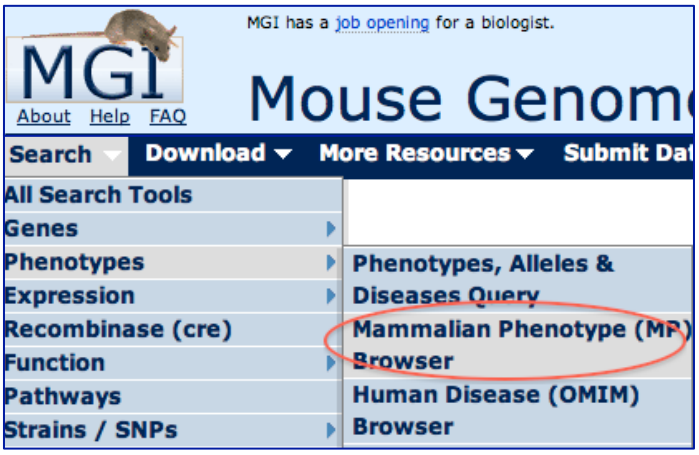
OMIM ID	Human Disease
211390	Sabinas Brittle Hair Syndrome
268700	Saccharopinuria
600145	Sacral Defect with Anterior Meningocele
101400	Saethre-Chotzen Syndrome; SCS (8 mouse models)
610871	Sakoda Complex
181010	Salivary Duct Calculi
181030	Salivary Gland Adenoma, Pleomorphic
180950	Salivary Substance, Clostridium Botulinum Type
268800	Sandhoff Disease (6 mouse models)
613005	Santos Syndrome
268850	Sao Paulo MCA/MR Syndrome
609464	Sarcoidosis, Early-Onset
181000	Sarcoidosis, Susceptibility to, 1; SS1
612387	Sarcoidosis, Susceptibility to, 2; SS2
612388	Sarcoidosis, Susceptibility to, 3; SS3
300813	Sarcoma, Synovial (3 mouse models)
268900	Sarcosinemia

The OMIM accession ID links to the OMIM database. The Human Disease term links to the MGI Human Disease and Mouse Model Detail page, like that for Papillorenal Syndrome on page 4 of this tutorial.

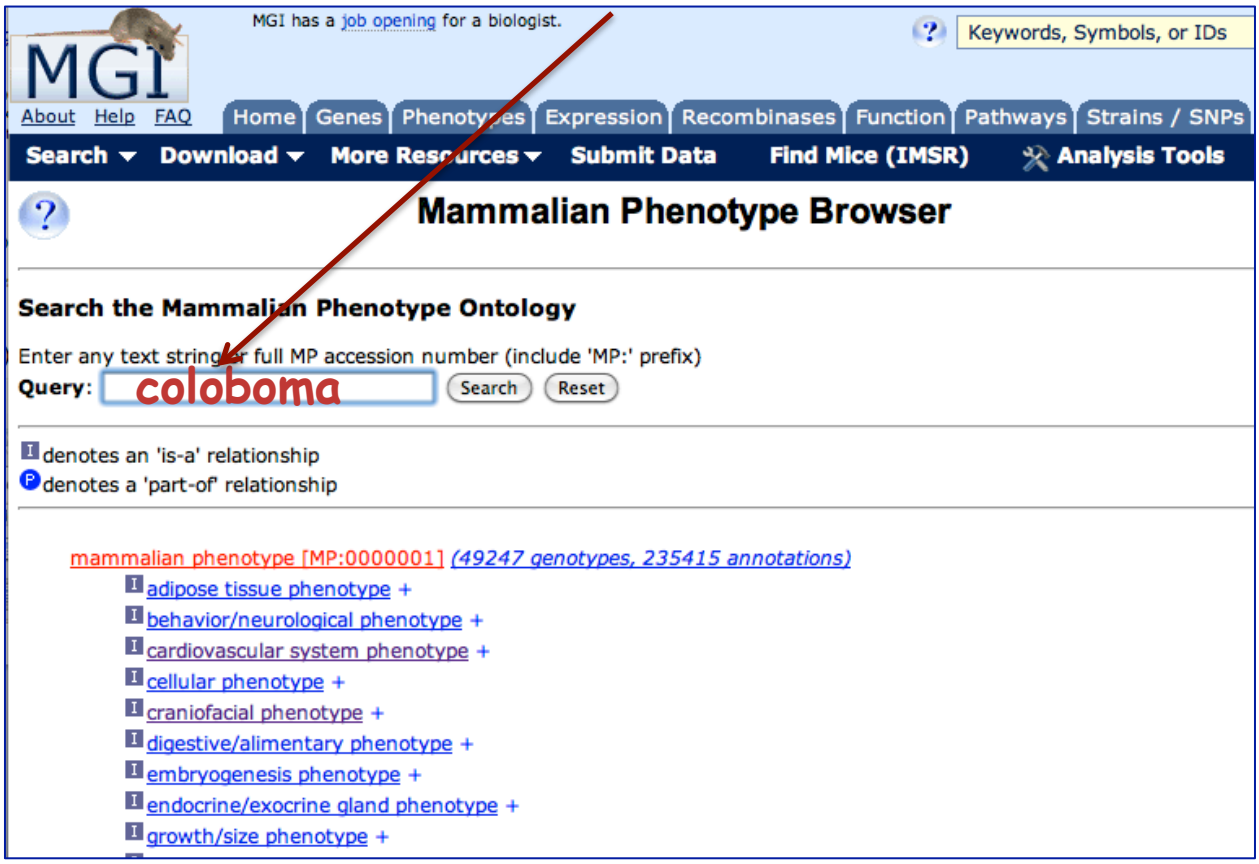
Searching by a Phenotypic Characteristic / Symptom

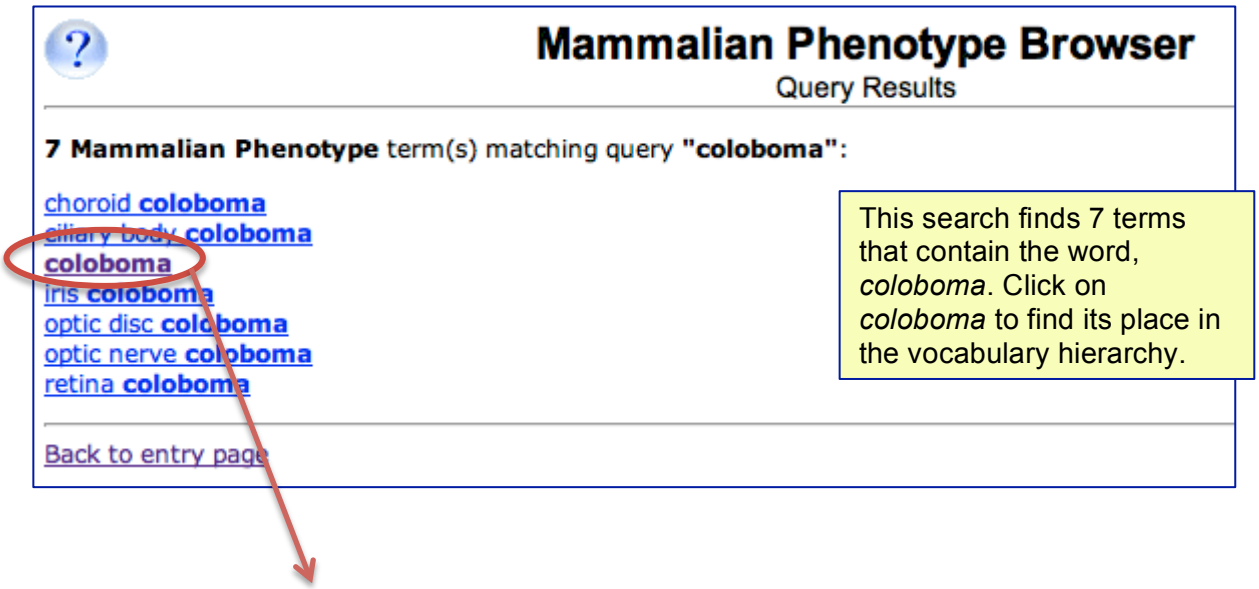
One of the phenotypic characteristics of Papillorenal Syndrome is *optic coloboma*. How can you find all mouse alleles associated with coloboma?

Go to the "Search" pull-down menu in the navy blue navigation bar along the top of any MGI page. Then select Mammalian Phenotype (MP) Browser from the Phenotypes section.

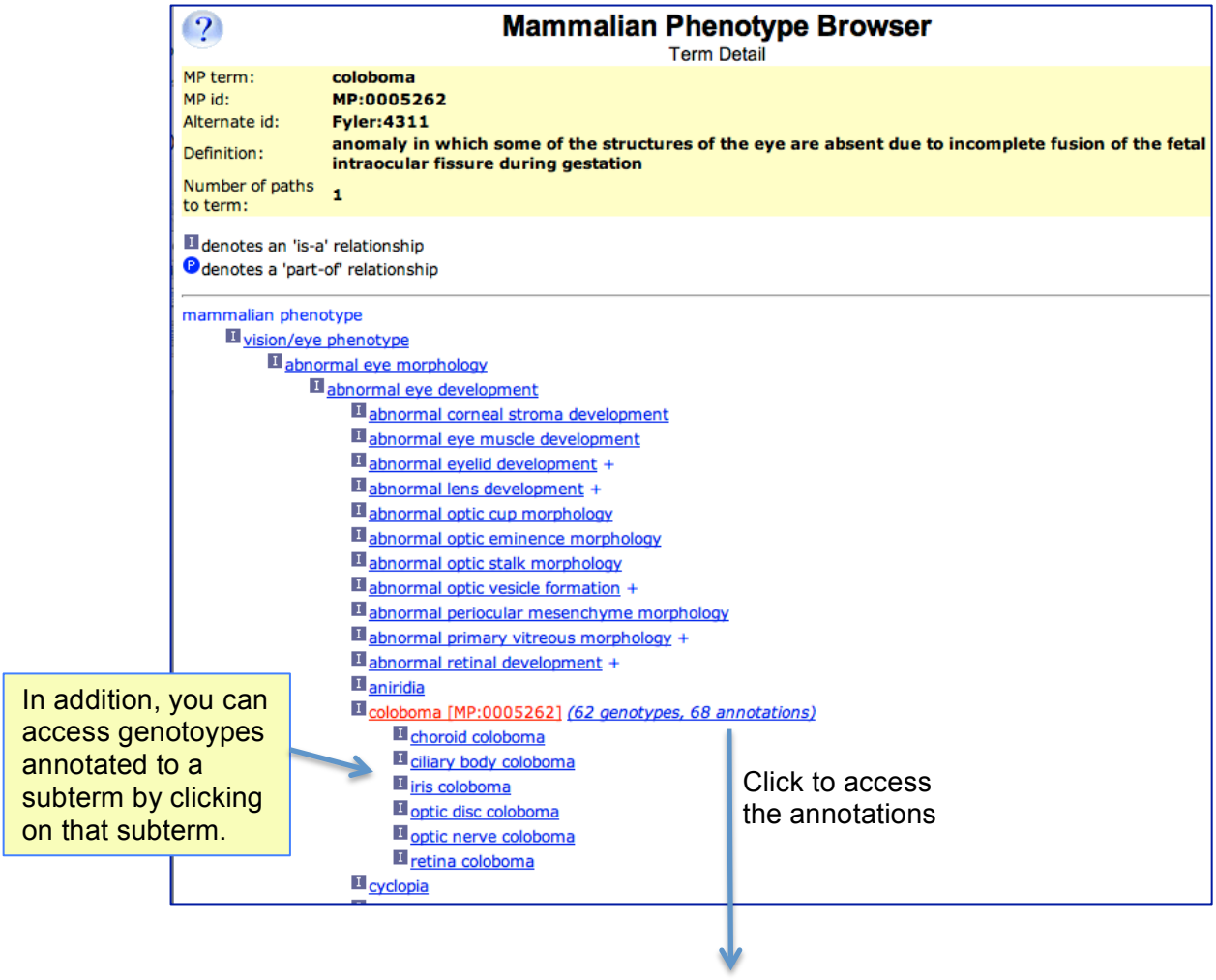


The Mammalian Phenotype Ontology has a hierarchical structure that permits a range of detail from high-level, broadly descriptive terms to very low-level, highly specific terms. The vocabulary can be searched or browsed. For this example, search for *coloboma*.





The results below for *coloboma* show the term's definition, its place in the full vocabulary hierarchy, sub-terms and a link to all the genotypes annotated to that term:



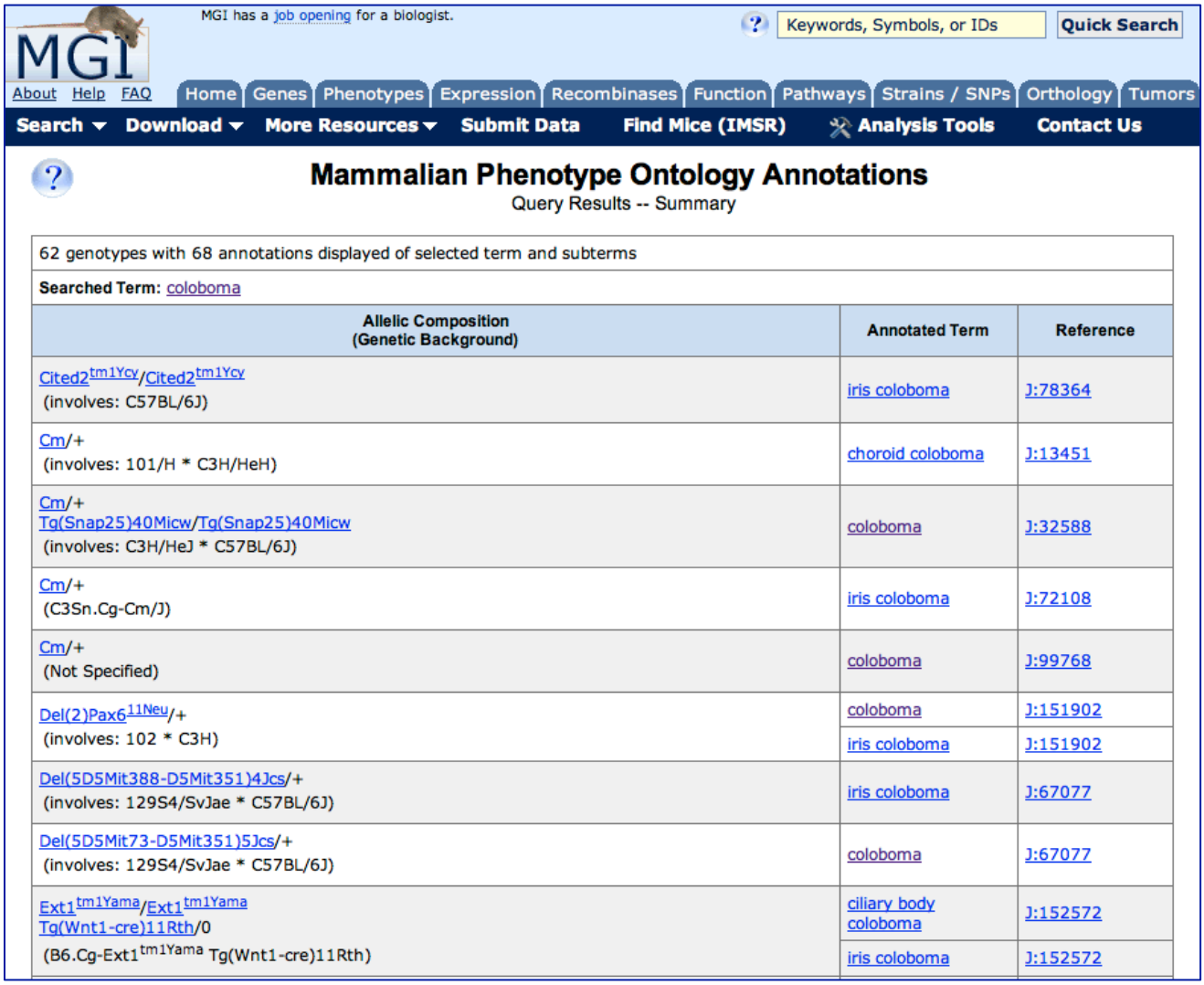
Below is a screenshot showing some of the annotations returned.

Genome-wide phenotypes

Note that the search just performed is for a *phenotype*, regardless of the genes involved; thus this search finds all mutant alleles *throughout the genome* that cause a given phenotype.

In this Annotations Page, the allele symbols (first column) link to the MGI allele detail pages, as shown previously in the *Pax2*^{M1Bpb} example on page 5 of this tutorial. The Annotated Term links to that term's place in the Mammalian Phenotype hierarchy, as in the previous figure on page 12, and the reference links to reference details.

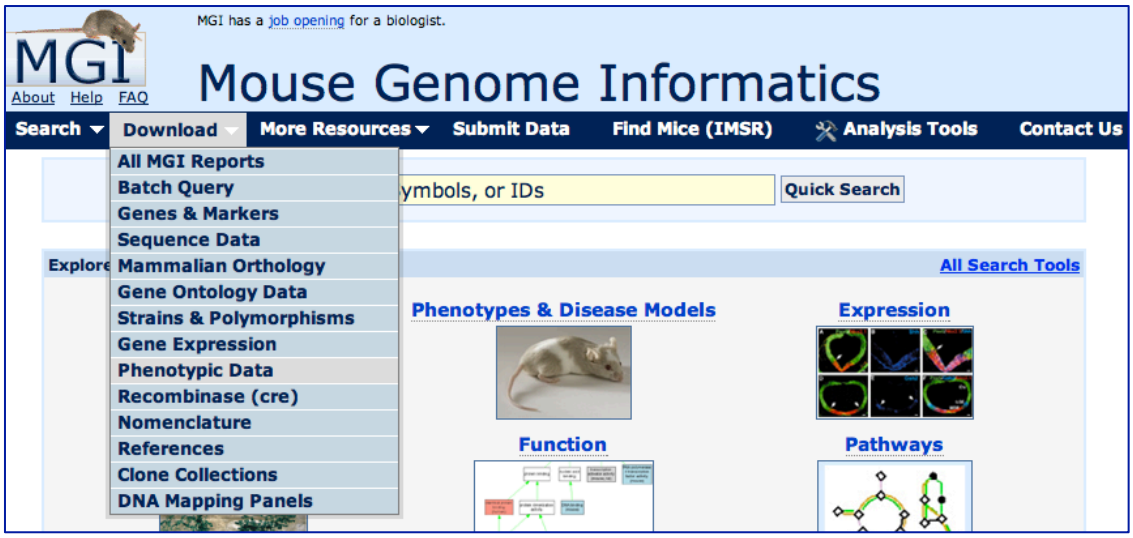
Note that the annotations returned are for those mouse mutations where the phenotype described is *coloboma* (the searched term) or any *sub-term of coloboma*. In the example below these include phenotypes of iris coloboma, choroid coloboma, and ciliary body coloboma, which are all “types” of coloboma.



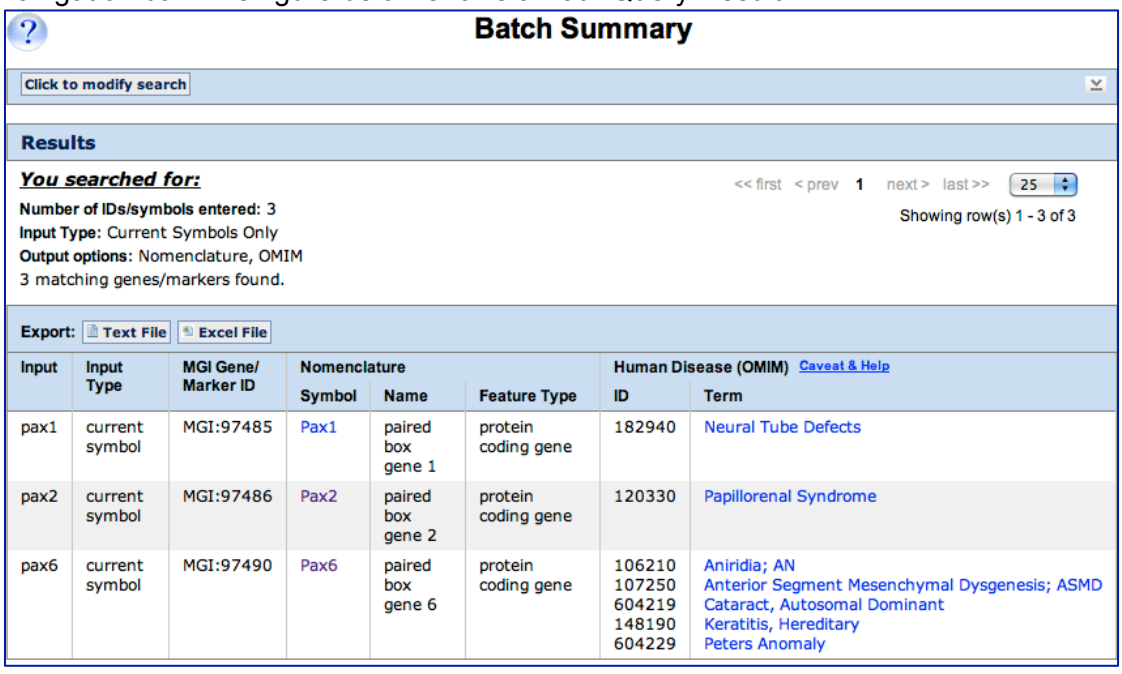
Retrieving sets of data on Mouse Models of Human Disease

For analysis or computational aggregation, users may want sets of data rather than details of single diseases, genes, or mutations. MGI provides three avenues for retrieving data sets:

1. Use the “Download” pull-down selection of the navy blue navigation bar to access weekly generated FTP files (standard reports) that include genes/alleles/phenotypes/human disease data.



2. MGI provides a Batch Query tool where input may be genes or various IDs, and, among other data types, associated diseases and phenotypes can be retrieved and exported as Text or Excel. The Batch Query is accessed under the “Search” pull-down section from the navy blue navigation bar. The figure below shows a Bath Query Result.



Batch Summary

Click to modify search

Results

You searched for:

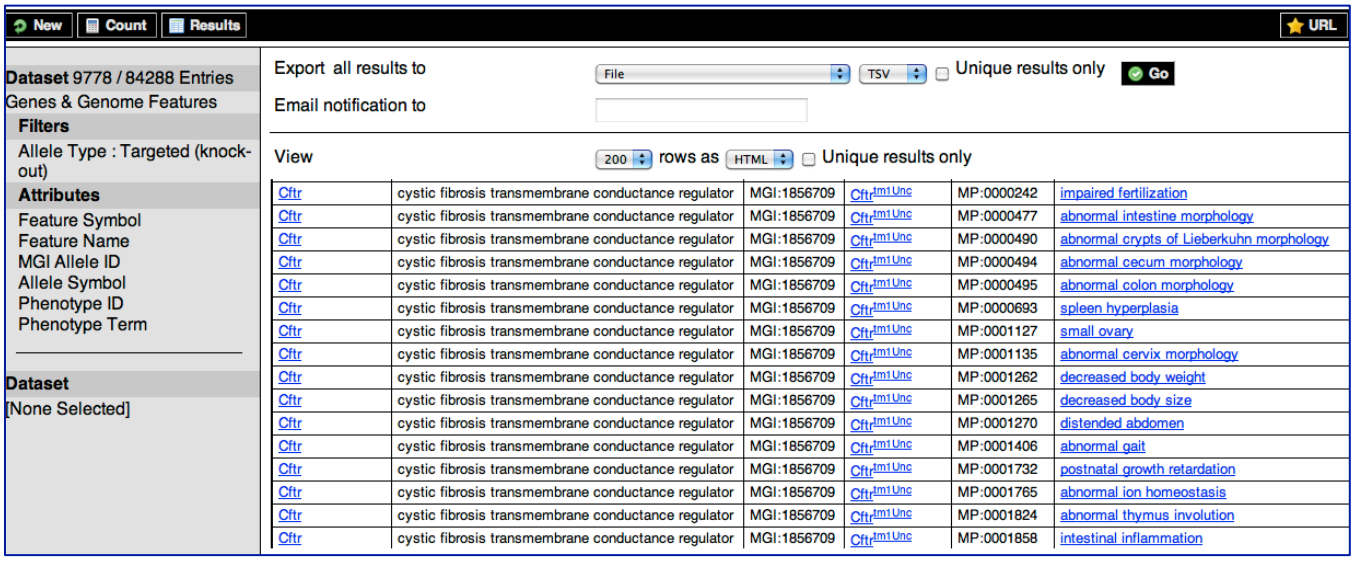
Number of IDs/symbols entered: 3
Input Type: Current Symbols Only
Output options: Nomenclature, OMIM
3 matching genes/markers found.

<< first < prev 1 next > last >> 25
Showing row(s) 1 - 3 of 3

Export: Text File Excel File

Input	Input Type	MGI Gene/ Marker ID	Nomenclature			Human Disease (OMIM) Caveat & Help	
			Symbol	Name	Feature Type	ID	Term
pax1	current symbol	MGI:97485	Pax1	paired box gene 1	protein coding gene	182940	Neural Tube Defects
pax2	current symbol	MGI:97486	Pax2	paired box gene 2	protein coding gene	120330	Papillorenal Syndrome
pax6	current symbol	MGI:97490	Pax6	paired box gene 6	protein coding gene	106210 107250 604219 148190 604229	Aniridia; AN Anterior Segment Mesenchymal Dysgenesis; ASMD Cataract, Autosomal Dominant Keratitis, Hereditary Peters Anomaly

3. The MGI BioMart tool allows selection of data filters and data attributes to produce files of customized content. Data may be exported as HTML, CSV, TSV, or Excel. Access the MGI BioMart from the “Search” pull-down section from the navy blue navigation bar. The figure below shows a BioMart Query Result.



Contact Us

We welcome questions and feedback. Contact us through the “Contact Us” link in the navy blue navigation bar at the far right of any MGI web page; or email us at mgi-help@jax.org