IMSR and MGI: 
tools moving research forward

Janan T. Eppig
Infrafrontier/IMPC workshop
Munich, May 2014
Where are the mouse resources I need?

In what state are they available (live, frozen embryos or Gametes, ES cell lines)?

How can I find more info about a strain or cell line?

How can I find more info about the mutations & alleles carried by a strain; and their phenotypes?

How can I order a mouse resource?

How can I contact the holding repository with other questions? (e.g. delivery times, cost)
Users (2013):
  • 58,800 unique users visited IMSR
  • Page views numbered >350,000 from 102 countries
## IMSR REPOSITORIES

<table>
<thead>
<tr>
<th>Repository / Consortium #</th>
<th>Abbreviation</th>
<th>REGION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australian Phenome Bank*</td>
<td>APB</td>
<td>Australia</td>
</tr>
<tr>
<td>Center for Animal Resources and Development</td>
<td>CARD</td>
<td>Japan</td>
</tr>
<tr>
<td>Canadian Mouse Mutant Repository</td>
<td>CMMR</td>
<td>Canada</td>
</tr>
<tr>
<td>European Mouse Mutant Archive*</td>
<td>EMMA</td>
<td>Europe</td>
</tr>
<tr>
<td>E.M. Simpson</td>
<td>EMS</td>
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<td>MRC Harwell</td>
<td>HAR</td>
<td>U.K.</td>
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<td>JAX Mice</td>
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<td>Knockout Mouse Project</td>
<td>KOMP</td>
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<tr>
<td>Mutant Mouse Regional Resource Centers*</td>
<td>MMRRC</td>
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<tr>
<td>MUGEN Mouse Database</td>
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<tr>
<td>National Cancer Institute at Frederick</td>
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<td>National Institute of Genetics</td>
<td>NIG</td>
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<tr>
<td>National Resource Center for Mutant Mice</td>
<td>NRCMM</td>
<td>China</td>
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<tr>
<td>Oriental BioService, Inc.</td>
<td>OBS</td>
<td>Japan</td>
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<td>Oak Ridge Collection at JAX</td>
<td>ORNL</td>
<td>U.S.A.</td>
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<td>National Applied Research Laboratories</td>
<td>RMRC-NLAC</td>
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<td>U.S.A.</td>
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<tr>
<td>Texas A&amp;M Institute for Genomic Medicine</td>
<td>TIGM</td>
<td>U.S.A.</td>
</tr>
<tr>
<td>Wellcome Trust Sanger Institute</td>
<td>WTSI</td>
<td>U.K.</td>
</tr>
</tbody>
</table>

* consortiums representing 4-14 individual repository sites (all repositories = 46)

# an additional 5 repositories have registered, but not yet submitted data
How do users get to IMSR to start with?

Where do users go once they find the resource they want?
Welcome to the IMSR

The IMSR is a searchable online database of mouse strains, stocks, and mutant ES cell lines available worldwide, including inbred, mutant, and genetically engineered strains. The goal of the IMSR is to assist the international scientific community in locating and obtaining mouse resources for research. Note that the data content found in the IMSR is as supplied by strain repository holders.

For each strain or cell line listed in the IMSR, users can obtain information about:
- Where that resource is available (Repository Site)
- What state(s) the resource is available as (e.g. live, cryopreserved embryo or germplasm, ES cells)
- Links to descriptive information about a strain or ES cell line
- Links to mutant alleles carried by a strain or ES cell line
- Links for ordering a strain or ES cell line from a Repository
- Links for contacting the Repository to send a query

Search for:

[Search] [Reset] [Hide Options]

Strain State: Any
- ES Cell
- embryo
- live
- ovaries

Strain Type: Any
- closed colony
- congenic strain
- consomic or chromosome substitution strain

Repository:
- APB (Australian Phenome Bank) Australia
- CARD (Center for Animal Resources and Development) Japan
- CMMR (Canadian Mouse Mutant Repository) Canada
- EM (European Mouse Mutant Archive) Germany
- EMS (Dr. Elizabeth M. Simpson, Ph.D.) Canada
- HAR (MRC Harwell) UK
- JAX (JAX Mice) USA
- KOMP (The Knockout Mouse Project) USA

Mutations:
- chemically induced mutation
- chromosomal aberration
- deletion
- duplication
- gene trap
- insertion
- inversion
- other
- radiation induced mutation
- reciprocal translocation
- recombination(cro/flip)
- robertsonian translocation
- spontaneous mutation
- targeted mutation
- transgenic

Available Strains by state

View Repository Reports.

All regions and repositories are selected by default; to limit your search to a specific region, click on the map, or select one or more specific repositories from the select list.
### Filters:
- Remove All Filters
- State: embryo
- State: sperm
- Provider: EM
- Provider: JAX

### Summary
2 item(s) match after applying filter(s).

#### Search for:
- **brc1**

#### You searched for:
- 125 strains(s) match your unfiltered search.

<table>
<thead>
<tr>
<th>N</th>
<th>Strain Name</th>
<th>Synonyms</th>
<th>States</th>
<th>Repository</th>
<th>Mutation Types</th>
<th>Alleles</th>
<th>Genes</th>
<th>Strain Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>FVB.129P2-Brca1&lt;sup&gt;tm1Bnn&lt;/sup&gt;/Chr2</td>
<td>FVB.129P2-Brca1&lt;sup&gt;tm1Bnn&lt;/sup&gt;/Ibcn, FVB.Cg-Brca1&lt;sup&gt;tm1Bnn&lt;/sup&gt;/Ibcn, Br1F</td>
<td>embryo</td>
<td>EM</td>
<td>targeted mutation</td>
<td>Brca1&lt;sup&gt;tm1Bnn&lt;/sup&gt;</td>
<td>Brca1&lt;sup&gt;1&lt;/sup&gt; breast cancer 1</td>
<td>mutant strain</td>
</tr>
<tr>
<td>+</td>
<td>STOCK Brca1&lt;sup&gt;tm1Aash&lt;/sup&gt;/J</td>
<td></td>
<td>embryo</td>
<td>JAX</td>
<td>targeted mutation</td>
<td>Brca1&lt;sup&gt;tm1Aash&lt;/sup&gt;</td>
<td>Brca1&lt;sup&gt;1&lt;/sup&gt; breast cancer 1</td>
<td>mutant stock</td>
</tr>
</tbody>
</table>

- Strain -> repository page
- Email + Order link
- Allele/phenotype (MGI)
- Gene page (MGI)
IMSR – going forward:

- infrastructure upgrade -> re-implement in PostgreSQL
- gene & allele search improvements
- follow-up with registered/not-submitted repositories
- ability to search MGI from within IMSR
Recent features Added to MGI

1. Re-designed phenotype data representation to integrate high-throughput phenotyping & multiple sites; prototype for anticipated IMPC data.

2. New for Cre Portal www.creportal.org
   • Matrix summary for cre tissue activity
   • Migrated to use EMAPA for tissue terms

3. New Human-Mouse Disease Connection (HMDC) Beta
   www.diseasemodels.org

4. Coming (May 22 release)
   • Re-implementation of allele categories
     • Allele generation type
     • Allele effect
     • Allele collections
Integrating high-throughput phenotype data with published and/or individual lab or consortium-submitted data.

MGI has integrated high-throughput phenotype data from the Wellcome Trust Sanger Institute (WTSI) and Europhenome (EuPh) and redesigned its web interface for Allele detail.

- Allows comparison between different Center’s data interpretation, where data are from the same genotypes/mice.

- Model built in anticipation of data being available from the phenotyping centers of the IMPC.

Implemented a Derivative Allele Load to assign ‘tm1b’ and other derivative alleles from the IMPC project and provide MGI_IDs and nomenclature to iMits.
**Spns2**<sup>tm1a(KOMP)Wtsi</sup>  
Targeted Allele Detail

### Nomenclature
- **Symbol:** Spns2<sup>tm1a(KOMP)Wtsi</sup>  
- **Name:** spinster homolog 2; targeted mutation 1a, Wellcome Trust Sanger Institute  
- **MGI ID:** MGI:4460276  
- **Gene:** Spns2  
  - **Location:** Chr11:72451638-72489904 bp, - strand  
  - **Genetic Position:** Chr11, 44.31 cM

### Mutation origin
- **Mutant Cell Lines:** EPD0090_5_A05, EPD0090_5_B04, EPD0090_5_C04, EPD0090_5_D06, EPD0090_5_E04, EPD0090_5_E05, EPD0090_5_E06, EPD0090_5_F04, EPD0090_5_F05, EPD0090_5_G04 (Wellcome Trust Sanger Institute)  
- **Germline Transmission:** Earliest citation of germline transmission: J:188933  
- **Parent Cell Line:** JM8.N19 (ES Cell)  
- **Strain of Origin:** C57BL/6N

### Mutation description
- **Allele Type:** Targeted (Floxed/Frt)  
- **Mutation:** Insertion  
  - **Vector:** L1L2_Bact_P  
- **Mutation details**

### Phenotypes
- **Key:**
  - hm: homozygous  
  - ht: heterozygous  
  - tg: involves transgenes  
  - cn: conditional genotype  
  - cx: complex: > 1 genome feature  
  - ot: other: hemizygous, indeterminate,...  
  - N: normal phenotype

#### Genotypes

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Allelic Composition</th>
<th>Genetic Background</th>
<th>Cell Line(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>hm1</td>
<td>Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;/Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;</td>
<td>C57BL/6-Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;</td>
<td>EPD0090_5_B04</td>
</tr>
<tr>
<td>hm2</td>
<td>Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;/Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;</td>
<td>Not Specified</td>
<td>EPD0090_5_B04</td>
</tr>
<tr>
<td>hm3</td>
<td>Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;/Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;</td>
<td>Not Specified</td>
<td>EPD0090_5_B04</td>
</tr>
<tr>
<td>ot4</td>
<td>Spns2&lt;sup&gt;tm1a(KOMP)Wtsi&lt;/sup&gt;/?</td>
<td>Not Specified</td>
<td>EPD0090_5_B04</td>
</tr>
</tbody>
</table>

#### Affected Systems
- **Behavior/neurological**  
- **Cardiovascular system**  
- **Hearing/vestibular/ear**  
- **Hematopoietic system**  
- **Homeostasis/metabolism**  
- **Increased circulating bilirubin level**  
- **Increased circulating glucose level**  
- **Immune system**  
- **Pigmentation**  
- **Skeletone**  
- **Vision/eye**
<table>
<thead>
<tr>
<th>Phenotypes:</th>
<th>Affected Systems</th>
<th>Sex:</th>
<th>Source:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>show or hide all annotated terms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sex:</td>
<td>MGI</td>
<td>WTSi</td>
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<tr>
<td>behavior/neurological</td>
<td></td>
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<tr>
<td>cardiovascular system</td>
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<tr>
<td>hearing/vestibular/ear</td>
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<td>hematopoietic system</td>
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<tr>
<td>homeostasis/metabolism</td>
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<tr>
<td>increased circulating bilirubin level</td>
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<tr>
<td>decreased circulating glucose level</td>
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<td>immune system</td>
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<td>pigmentation</td>
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<tr>
<td>skeleton</td>
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<td></td>
</tr>
<tr>
<td>vision/eye</td>
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</tr>
</tbody>
</table>

Homeostasis / metabolism phenotypes only scored as significant by Sanger; not Europhenome
Cre Portal Enhancements
www.creportal.org & linked from the MGI homepage

1. Searches for recombinase activity now provide autocomplete function for choosing tissue terms from EMAPA (release May 22)

1. The recombinase allele detail pages show a summary matrix of age and structure where activity was detected/not detected

1. Your Observations Welcome button allows the community to report unexpected findings, e.g. unpublished off-target activity
Recombinase (cre) Activity

MG1 collects and annotates expression and activity data for recombinase-containing transgenes and knock-in alleles.

Access Data

Find recombinase-carrying alleles

Search for alleles assayed for specificity/activity in an anatomical structure.

Recombinase activity in:

left atrium
left atrium left atrium cardiac muscle
left atrium cardiac muscle left atrium endocardial lining
left atrium endocardial lining
left atrium auricular region
left atrium auricular region cardiac muscle
left atrium auricular region cardiac muscle
common atrial chamber left part
common atrial chamber left part cardiac jelly
common atrial chamber left part cardiac muscle
common atrial chamber left part common atrial chamber left endocardial lining

Retrieval

Retrieve

FAQs

How do I...

...find existing recombinase-expressing transgenes and knock-ins that have a given promoter (driver)?

FAQ

* Release May 22

Autocomplete terms using EMAPA

Bold emphasis on searched anatomical system

Recombinase Alleles - Tissue Summary

You searched for:
Activity assayed in left atrium cardiac muscle
includes synonyms & substructures
System(s) in bold contain matching search terms.
Click column headings to sort table data.

<table>
<thead>
<tr>
<th>Driver</th>
<th>Allele Symbol</th>
<th>Gene, Allele Name</th>
<th>Recombinase Activity Detected</th>
<th>Recombinase Activity Not Detected</th>
<th>Allele Synonym</th>
<th>Inducible</th>
<th>Find Mice (M3R)</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>My/h6</td>
<td>Tg(Myh6-cre)2182Mds</td>
<td>transgene insertion 2182, Michaela Schneider</td>
<td>alimentary system, cardiovascular system, hemodmphoid system, renal and urinary system, reproductive system, respiratory system</td>
<td>Imbs, liver and biliary system</td>
<td>MCH-cre, MHC-Cre, MHCalphaCre, MHC-Cre, Tg(Myh6-cre)2182Mds, alpha-MHC-Cre, alphaMHC-Cre, alphamyHC-Cre</td>
<td>3</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>W11</td>
<td>Wt1CreERT2(Wap)</td>
<td>Wilms tumor 1 homodip; targeted mutation 2, William T. Pu</td>
<td>cardiovascular system, cavities and their linings</td>
<td></td>
<td>Wt1CreERT2, Wt1Cre (t represents inducible, Wt1Cre)</td>
<td>Yes</td>
<td>16</td>
<td></td>
</tr>
</tbody>
</table>
Cre Transgene Detail showing matrix summary of Activity in Tissue Systems x Age

**Tg(Myh6-cre)2182Mds**

**Nomenclature**
- Symbol: Tg(Myh6-cre)2182Mds
- Name: transgene insertion 2182, Michael D Schneider
- MGI ID: MGI:2386742
- Synonyms: alphaMhc-Cre, alpha-MHC-Cre<sup>+</sup>, alphaMyHC-Cre, MCH-cre, MHCalphaCre, MHCre, MHC-Cre, Tg(Myhca-cre)2182Mds
- Transgene: Tg(Myh6-cre)2182Mds Location: unknown

**Transgene origin**
- Strain of Origin: FVB/N

**Transgene description**
- Transgene Type: Transgenic (Recombinase)
- Mutation: Insertion
  - Mutation details

**Recombinase activity**
- Activity: Activity in Systems/Structures
  - **show or hide all structures**
  - **Activity Detected**
  - **Activity Not Detected**
  - **E 0-8.9**
  - **E 9.0-13.9**
  - **E 14-19.5**
  - **P 0-21**
  - **Post-weaning P 22-42**
  - **Adult >P 43**

- **Activity in Systems/Structures**
  - **alimentary system**
  - **cardiovascular system**
  - **hemolymphoid system**
  - **limbs**
  - **liver and biliary system**
  - **renal and urinary system**
  - **reproductive system**
  - **respiratory system**

**Driver:** Myh6 Summary of all recombinase alleles driven by Myh6.

*Your Observations Welcome*
# Tg(Myh6-cre)2182Mds - Cardiovascular System

## Recombinase Activity Detail

<table>
<thead>
<tr>
<th>Allele Information</th>
<th>Tissue Information</th>
<th>Images</th>
<th>Recombinase Activity</th>
<th>References</th>
</tr>
</thead>
</table>

### Allele Information

- **Allele:** Tg(Myh6-cre)2182Mds
  - transgene insertion 2182, Michael D Schneider
- **Synonym:** alphaMhc-Cre, alpha-MHC-Cre<sup>+</sup>, alphaMyHC-Cre, MCH-cre, MHCalphaCre, MHCcre, MHC-Cre, Tg(Myhca-cre)2182Mds
- **Molecular description:** The transgenic construct contained the Myh7 3' untranslated region, the Myhca promoter, Myhca noncoding exons 1 and 2 driving the expression of the cre recombinase sequence. The Myhca promoter drives expression in cardiac tissue.
- **Find mice (IMSR):** Mouse Strains: 3 strains available
- **Cell Lines:** 0 lines available
- **Additional Tissues:** Tg(Myh6-cre)2182Mds activity also observed in: alimentary system, hemolymphoid system, renal and urinary system, reproductive system, respiratory system.

### Tissue Information

**Cardiovascular System**

Other recombinase alleles with activity in Cardiovascular System tissues: 1700009P17Rik<sup>tm1.1(cre)Hel</sup>, Calb2<sup>tm1(cre)Zjh</sup>, Cck<sup>tm1.1(cre)Zjh</sup>, Crh<sup>tm1(cre)Zjh</sup> ...(more)

### Images

Drag images to compare to others or to data in the table below. Drag corners to resize images for more detail. **Reset Images**
Human-Mouse Disease Connection
www.diseasemodels.org

version released

Search by: human or mouse gene
human or mouse genome location
phenotype or disease term
submitted VCF file

Provide overview of human/mouse data incorporating phenotypes and disease
- Grid overview
- Gene-based Summary
- Disease-based Summary

Drill down to
- Genotypes (allele composition) profile of phenotypes → detailed pheno data
- Links to IMSR
Spotlight on mouse models of human disease

**Human T-Cell Immunodeficiency, Congenital Alopecia, and Nail Dystrophy (OMIM: 601705)**

Humans and mice homozygous for recessive mutations in the FOXN1 (forkhead box N1) gene display common phenotypes:

- congenital alopecia
- absent thymus
- severe T-cell immunodeficiency
- nail dystrophy
- limited lifespan

[Read more...]
You searched for: Phenotypes or Diseases matching [105830(Angelman Syndrome; AS),]

Showing results(s) 1 - 4 of 4

Legend:
- Terms are annotated to genes in **human/mouse**. Darker colors indicate [more annotations](#).

N - No abnormal phenotype observed.

**NOTE:** Searching by phenotype/disease term restricts the gene results based on the search term. Search by gene or genome location for the complete phenotype profile of gene mutations. [More..](#)

<table>
<thead>
<tr>
<th>Human Gene</th>
<th>Mouse Gene</th>
<th>adipose tissue</th>
<th>behavior/neurological</th>
<th>cellular</th>
<th>growth/size</th>
<th>homeostasis/aging</th>
<th>nervous system</th>
<th>reproductive system</th>
<th>Angelman Syndrome; AS</th>
<th>Prader–Willi Syndrome; PWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNRPN</td>
<td>Snrpn</td>
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<td>UBE3A</td>
<td>Ube3a</td>
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</tbody>
</table>
### Data for Ube3a and nervous system abnormalities

Find Mice: IMSR strains or lines carrying any Ube3a Mutation (18 available).

- Aspects of the system are reported to show a normal phenotype
- Indicates phenotype varies with strain background

<table>
<thead>
<tr>
<th>Mouse Genotype</th>
<th>audiogenic seizures</th>
<th>tonic-clonic seizures</th>
<th>absence seizures</th>
<th>abnormal spike wave discharge</th>
<th>increased dopamine level</th>
<th>abnormal brain weight</th>
<th>abnormal cerebral cortex morph.</th>
<th>small cerebellum</th>
<th>abnormal dendrite morphology</th>
<th>abnormal nervous system elect.</th>
<th>abnormal brain wave pattern</th>
<th>reduced long term potentiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ube3atm1Alb/Ube3a+</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Ube3atm1Jw/Ube3a+</td>
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</tbody>
</table>

Link to IMSR page displaying 18 available resources carrying *Ube3a* mutations

Link to MGI detailed phenotype descriptions for *Ube3a*<sup>tm1Alb</sup>/Ube3a+ heterozygotes.
MGI—going forward:

- Further development of the Human-Mouse Disease Connection site
  - human phenotypes from HPO
  - synteny map displays for regions
  - more data filtering options (e.g. types of loci, delete/retain grid columns/rows)
  - accept additional file input formats
  - for VCF files, return file annotated with identified genes+
  - enhance Boolean search capabilities

- Incorporate IMPC data (awaiting IMPC release)

- ‘Relationship’ project
  - microRNA targets (experimental and predicted)
  - genomic content of cluster regions
  - ‘genomic mutation’ content
IMSR : International Mouse Strain Resources
www.findmice.org

MGI: Mouse Genome Informatics
www.informatics.jax.org

HMDC: Human-Mouse Disease Connection
www.mousemodels.org

CrePortal:
www.creportal.org