The IMPC: Building the First Comprehensive Catalog of a Mammalian Genome

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Part of the MPI2 consortium

www.mousephenotype.org
CREATE
20,000 knockout mouse strains – one null mutant mouse line for each protein coding gene

CHARACTERIZE
Systematically phenotype each strain

CATALOGUE
Make mutant strains publicly available
Publish data in near real time & provide analysis tools

CONNECT
Link phenotypic data to known biology
Disease models
Background: Building on IKMC Success

International Knockout Mouse Consortium

NIH: Knockout Mouse Program (KOMP1)

EU: European Conditional Mouse Mutagenesis Program (EUCOMM)

Genome Canada: North American Conditional Mouse Mutagenesis Project (NorCOMM)

Texas A&M: Texas A&M Institute for Genomic Medicine (TIGM)

EUCOMM - Tools for Functional Annotation of the Mouse Genome

IMPC
Background: Building on IKMC Success

>15,000 targeted mutant alleles created in C57BL/6N ES cell lines and more coming
Background: The IMPC

International Mouse Phenotype Consortium

- Create and Characterize 20,000 knockout lines over 10 years
- Phase 1- 5000 strains by 2016
- Publish & Annotate Data in near Real-Time
- Integrate IMPC data with human mutation and disease repositories
CHARACTERIZE- High quality data
CREATE: Knockout Line Production

KOMP
Velicogene

EUCOMM

IMPC

DEMO I
We are building the first truly comprehensive, functional catalogue of a mammalian genome.

The Knockout Mouse
A powerful tool for precision medicine.

Learn more

Search IMPC database

Enter your favorite gene, phenotype, anatomy or protocol to find IMPC data important to your research.

Or browse

new gene-phenotype associations

mousephenotype.org
We are building the first truly comprehensive, functional catalogue of a mammalian genome.

The Knockout Mouse
A powerful tool for precision medicine.

International Mouse Phenotype Consortium

The goal of the International Mouse Phenotyping Consortium (IMPC) is to discover functional insight for every gene by generating and systematically phenotyping 20,000 knockout mouse strains.

One of the most important tools at our disposal in understanding mammalian gene function is the laboratory mouse. The fundamental genetic similarity between mice and humans allows researchers to infer a human gene’s function based on studies with laboratory mice. One powerful technique is to turn off, or “knockout”, the activity of a mouse gene to assess what biological systems are impacted. This gives insights how a similar gene in humans may contribute to disease when its activity is altered.

The IMPC is generating a knockout mouse strain for every protein coding gene by using the embryonic stem cell resource generated by the International Knockout Mouse Consortium (IKMC). The production of mouse strains from these ES cells are tracked within the "international Micro-injection tracking system" (IMits) and are made available to the research community via public repositories.

Systematic broad-based phenotyping is performed by each IMPC center using standardized procedures found within the International Mouse Phenotyping Resource of Standardised Screens (IMPreSS) resource. Gene-to-phenotype associations are made by a versioned statistical analysis with all data freely available via the web portal and by several data download features.

IMITS is the designated planning and tracking resource for IMPC mutant mouse strain production.

Visit IMITS
**CREATE: Knockout Line Production**

iMits website reports real-time production status

<table>
<thead>
<tr>
<th>Status</th>
<th>Current Total (up to and Inc. May)</th>
<th>Last Complete Month (May)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All genes</td>
<td>1379</td>
<td>55</td>
</tr>
<tr>
<td>E5. Cell QC (genes)</td>
<td>877</td>
<td>26</td>
</tr>
<tr>
<td>E5 QC Confirmed (genes)</td>
<td>795</td>
<td>26</td>
</tr>
<tr>
<td>E5 QC Failed (genes)</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Microinjections (genes)</td>
<td>831</td>
<td>27</td>
</tr>
</tbody>
</table>

To date:
- 7000 ES clones have been injected
- 3000 genotype confirmed
- 1600 cre excised
We are building the first truly comprehensive, functional catalogue of a mammalian genome.

The Knockout Mouse
A powerful tool for precision medicine.
[Read why]

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IMPReSS contains standardized phenotyping protocols, essential for the characterization of mouse phenotypes.
[Visit IMPReSS]

iMITS
IMITS is the designated planning and tracking resource for IMPC mutant mouse strain production.
[Visit IMITS]
CHARACTERIZE
Adult phenotypes

• IMPReSS: (International Mouse Phenotyping Resource of Standardised Screens)
• Ascribe Biological Function to Each Gene
• Collaborate with phenotyping specialists
**Characterize**

- **Protocol**

  ![Clinical Blood Chemistry](image)

  **Purpose**
  Clinical chemistry determines biochemical parameters in plasma including enzymatic activity, specific substrates and electrolytes.

  **Experimental Design**
  Minimum number of mutant animals; must maintain it 7 size for male and female.

  Age of animals: 18 weeks

  Sexual dimorphism: Yes for some of the parameters.

- **Data Parameter**

  ![Table of Parameters](image)

- **Ontology**

  ![Parameter: Sodium IMPC_CBC_001_001](image)

  **Parameter: Sodium IMPC_CBC_001_001**

<table>
<thead>
<tr>
<th>Option</th>
<th>Increment</th>
<th>Ontology Term</th>
<th>Ontology ID</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCREASED</td>
<td></td>
<td>increased circulating sodium level</td>
<td>MP:0005633</td>
<td></td>
</tr>
<tr>
<td>DECREASED</td>
<td></td>
<td>decreased circulating sodium level</td>
<td>MP:0005634</td>
<td></td>
</tr>
<tr>
<td>ABNORMAL</td>
<td></td>
<td>abnormal circulating sodium level</td>
<td>MP:0001776</td>
<td></td>
</tr>
</tbody>
</table>
A third of lines will be embryonic lethal
Specialized pipeline created
Cutting-edge imaging technologies being employed
IMPReSS API Access

• IMPReSS is accessible programmatically utilising a SOAP web service.

• This API access exposed all the Pipeline, Procedure, Parameter and Ontology term information held within IMPReSS

• The WSDL is available at https://www.mousephenotype.org/impress/soap/server?wsdl

• With full documentation available at https://www.mousephenotype.org/impress-web-services-technical-description
CHARACTERIZE- High quality data
CHARACTERIZE- Ensuring High quality Data

• All data **visually QCd** by the DCC Data Wranglers
  
  • Identify biologically impossible errors in data
  
  • Standardised protocols adhered to in each centre

• Monthly report to all centres:
  
  ▪ Update on QC progress (number of issues raised vs resolved)
  
  ▪ Draw attention to ongoing data problems, e.g. low cohort size

• Interactive QC system:
  
  ▪ wranglers raise QC queries (“issues”) - centre responds
CHARACTERIZE- Shared QC interface
CHARACTERIZE- STATS Analysis
CHARACTERIZE- PhenStat
Our production statistical analysis

• Associate Genotype to Phenotype
  • Multiple workflows
  • Multiple data types
  • Built statistical analysis platform on expected workflows
    • Fisher Exact Test, Linear regression- Mixed Model

• The PhenStat package
What is PhenStat?

- Freely available R Package
- Version controlled
- Multiple workflows
- Can include a covariate e.g. body weight.
- Gives both a statistical and biological measure
- Assesses sexual dimorphism
Statistical benefits include:

- Various statistical strategies implemented
- Can include a covariate e.g. body weight.
- Gives both a statistical and biological measure
- Assesses sexual dimorphism
CHARACTERIZE- Other Approaches (BAYESIAN)

- Non-Gaussian response distributions
- Correlated observations (same litter, same day measured)
- Effects of measured variables
  - Biological variation e.g. sex or mouse strain.
  - Experimental effects, e.g. investigator
  - *model as covariates*
- Effects of unmeasured variables
  - Systematic drift over time in baseline mean or variance
  - Clustering of baseline response not explained by metadata
  - *Address systematic baseline drift by incorporating a smooth function of time in the model*
CHARACTERIZE- Other Approaches (BAYESIAN) II

• Unified approach to quantitative and categorical data
  • Linear regression on transformed quantitative data
  • Logistic regression on categorical data

• Known sources of variation modelled as covariates
  • Day, litter, sex, strain, experimenter, metadata

• Effects of unmeasured variables
  • Address systematic baseline drift by incorporating a smooth function of time in the model
DEMO II
Follow genes you are interested in. IMPC will send an email when new data is published.
Search for a specific gene, type of gene, phenotype, procedure or phrase

Example Searches

Sample queries for several fields are shown. Click the desired query to execute any of the samples. Note that queries are focused on Relationships, leaving modifier terms to be applied as filters.

Gene query examples
Akt2 - looking for a specific gene, Akt2
*rik - looking for all Riken genes
hox* - looking for all hox genes

Phenotype query examples
abnormal skin morphology - looking for a specific phenotype
ear - find all ear related phenotypes

Procedure query Example
grip strength - looking for a specific procedure

Phrase query Example
zinc finger protein - looking for genes whose product is zinc finger protein
SEARCH

Filter your search

Genes

Phenotypes

- adipose tissue
- behavior/neurological
- cardiovascular system
- craniofacial
- embryogenesis
- endocrine/exocrine gland
- growth/size/body
- hearing/vestibular/ear
- hematopoietic system
- homeostasis/metabolism
- immune system
- integument
- limbs/digits/tail
- mortality/aging

Phenotype

- **decreased circulating glucose level**
  - Definition: less than the normal concentration in the blood of this major monosaccharide of the body; it is an important energy source

- **abnormal glucose homeostasis**
  - Definition: anomaly in the processes involved in the maintenance of an internal equilibrium of glucose in the fluids and tissues

- **abnormal circulating glucose level**
  - Definition: any anomaly in the concentration in the blood of the major monosaccharide of the body

Found 23 phenotypes

View example search

Download
Filter by phenotype, source, or pathology.

Filter your search

- Genes: 49495
- Phenotypes: 607
- Diseases: 7137
- Anatomy: 382
- Procedures: 4540
- Images: 100126

Found 22 genes
CONNECT- Gene page

Gene: Nbeal2

Name: neurobeachin-like 2
MGI Id: MGI:2448554

Status:
- ES cells
- Mice tm1a
- Mice tm1e
- Phenotype data available

ENSEMBL Links:
- Gene View
- Location View
- Compara View

Gene Summary at top of page
Phenotype associations for Nbeal2

Phenotype Summary based on automated MP annotations supported by experiments on knockout mouse models.

Both sexes have the following phenotypic abnormalities

- skeleton phenotype. Evidence from IMPC (3)
- hematopoietic system phenotype. Evidence from IMPC (5)

Following phenotypic abnormalities occurred in males only

- immune system phenotype. Evidence from IMPC (1)
### CONNECT - Gene to phenotype

#### Nbeal2

<table>
<thead>
<tr>
<th>Mouse anatomical entity</th>
<th>Pigmentation</th>
<th>Nervous system</th>
<th>Renal / urinary system</th>
<th>Limbs / digits / tail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nbeal2</td>
<td>0.75092</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adipose tissue</th>
<th>Homeostasis / metabolism</th>
<th>Hearing / vestibular / ear</th>
<th>Growth / size</th>
<th>Craniofacial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nbeal2</td>
<td>0.16142</td>
<td>0.00038938</td>
<td>0.0055548</td>
<td>0.045779</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiovascular system</th>
<th>Behavior / neurological</th>
<th>Immune system</th>
<th>Respiratory system</th>
<th>Reproductive system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nbeal2</td>
<td>0.044006</td>
<td>0.0025280</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Skeleton</th>
<th>Vision / eye</th>
<th>Other</th>
<th>Hematopoietic system</th>
<th>Mortality / aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nbeal2</td>
<td>0.0000060171</td>
<td>0.000033483</td>
<td>0.0062900</td>
<td>2.1094e-15</td>
</tr>
</tbody>
</table>

The phenotype heatmap illustrates the significance of gene expression changes across various anatomical and physiological systems.
### CONNECT- Gene to phenotype

- **Drill down further for detailed phenotype data**

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Allele</th>
<th>Zygosity</th>
<th>Sex</th>
<th>Procedure Parameter</th>
<th>Phenotyping Center</th>
<th>Source</th>
<th>P Value</th>
<th>Graph</th>
</tr>
</thead>
<tbody>
<tr>
<td>increased mean platelet volume</td>
<td>Nbea12&lt;sup&gt;tm1aj(EUCOMM)Wtsi&lt;/sup&gt;</td>
<td>homozygote</td>
<td>♂</td>
<td>Hematology</td>
<td>WTSI</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>decreased platelet cell number</td>
<td>Nbea12&lt;sup&gt;tm1aj(EUCOMM)Wtsi&lt;/sup&gt;</td>
<td>homozygote</td>
<td>♂</td>
<td>Hematology</td>
<td>WTSI</td>
<td>IMPC</td>
<td>2.11E-15</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>increased leukocyte cell number</td>
<td>Nbea12&lt;sup&gt;tm1aj(EUCOMM)Wtsi&lt;/sup&gt;</td>
<td>homozygote</td>
<td>♂</td>
<td>Hematology</td>
<td>WTSI</td>
<td>IMPC</td>
<td>4.71E-8</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>decreased bone mineral density</td>
<td>Nbea12&lt;sup&gt;tm1aj(EUCOMM)Wtsi&lt;/sup&gt;</td>
<td>homozygote</td>
<td>♂</td>
<td>Body Composition (DEXA lean/fat)</td>
<td>WTSI</td>
<td>IMPC</td>
<td>4.18E-6</td>
<td><img src="image" alt="Graph" /></td>
</tr>
</tbody>
</table>
## CONNECT - Display of data

### Allele - Nbeal2\textsuperscript{tm1a(EUCOMM)Wtsi}

<table>
<thead>
<tr>
<th>P Value</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1094E-15</td>
<td>Different effect size, males greater</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Sex*Genotype P Value</th>
<th>Effect size</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>7.1758E-22</td>
<td>-534.08</td>
<td>± 54.458</td>
</tr>
<tr>
<td>Male</td>
<td>9.1166E-38</td>
<td>-737.84</td>
<td>± 55.404</td>
</tr>
</tbody>
</table>
### CONNECT - Data in near real time

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Allele</th>
<th>Zygosity</th>
<th>Sex</th>
<th>Procedure</th>
<th>Parameter</th>
<th>Phenotyping Center</th>
<th>Source</th>
<th>P Value</th>
<th>Graph</th>
</tr>
</thead>
<tbody>
<tr>
<td>abnormal bone structure</td>
<td>Dnase112tm1.1(KOMP)Wtsi</td>
<td>heterozygote</td>
<td>♂</td>
<td>Body Composition (DEXA lean/fat)</td>
<td>Bone Area (BMC/BMD)</td>
<td>JAX</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="https://example.com/graph" alt="graph" /></td>
</tr>
<tr>
<td>abnormal bone structure</td>
<td>Dnase112tm1.1(KOMP)Wtsi</td>
<td>heterozygote</td>
<td>♂</td>
<td>Body Composition (DEXA lean/fat)</td>
<td>Bone Area (BMC/BMD)</td>
<td>UC Davis</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="https://example.com/graph" alt="graph" /></td>
</tr>
<tr>
<td>decreased body length</td>
<td>Dnase112tm1.1(KOMP)Wtsi</td>
<td>heterozygote</td>
<td>♂</td>
<td>Body Composition (DEXA lean/fat)</td>
<td>Body length</td>
<td>UC Davis</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="https://example.com/graph" alt="graph" /></td>
</tr>
<tr>
<td>decreased body weight</td>
<td>Dnase112tm1.1(KOMP)Wtsi</td>
<td>homozygote</td>
<td>♂</td>
<td>Grip Strength</td>
<td>Body weight</td>
<td>MRC Harwell</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="https://example.com/graph" alt="graph" /></td>
</tr>
</tbody>
</table>
Pheno-DCC- Pre QC view
X-Ray Images Lateral
LacZ Images
CONNECT- Find resources

Order Mice & ES Cells directly from website
CONNECT- Phenotype Pages

<table>
<thead>
<tr>
<th>Gene / Allele</th>
<th>Zygosity</th>
<th>Sex</th>
<th>Phenotype</th>
<th>Procedure Parameter</th>
<th>Phenotyping Center</th>
<th>Source</th>
<th>P Value</th>
<th>Graph</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankr13a</td>
<td>homozygote</td>
<td>♀</td>
<td>increased platelet cell number</td>
<td>Haematology</td>
<td>WTSI</td>
<td>EuroPhenome</td>
<td>0.0</td>
<td><img src="image1" alt="Ankr13a Link" /></td>
</tr>
<tr>
<td>Ghrhr</td>
<td>homozygote</td>
<td>♀</td>
<td>decreased platelet cell number</td>
<td>Hematology</td>
<td>JAX</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="image2" alt="Ghrhr Link" /></td>
</tr>
<tr>
<td>Nbeal2</td>
<td>homozygote</td>
<td>♀</td>
<td>increased mean platelet volume</td>
<td>Hematology</td>
<td>WTSI</td>
<td>IMPC</td>
<td>0.0</td>
<td><img src="image3" alt="Nbeal2 Link" /></td>
</tr>
<tr>
<td>Knstrm</td>
<td>homozygote</td>
<td>♀</td>
<td>decreased platelet cell number</td>
<td>Hematology</td>
<td>ICS</td>
<td>IMPC</td>
<td>1.11E-16</td>
<td><img src="image4" alt="Knstrm Link" /></td>
</tr>
<tr>
<td>Nbeal2</td>
<td>homozygote</td>
<td>♀</td>
<td>decreased platelet cell number</td>
<td>Hematology</td>
<td>WTSI</td>
<td>IMPC</td>
<td>2.11E-15</td>
<td><img src="image5" alt="Nbeal2 Link" /></td>
</tr>
<tr>
<td>Fbxo7</td>
<td>homozygote</td>
<td>♀</td>
<td>increased platelet cell number</td>
<td>Hematology</td>
<td>WTSI</td>
<td>IMPC</td>
<td>6.46E-12</td>
<td><img src="image6" alt="Fbxo7 Link" /></td>
</tr>
<tr>
<td>Crif3</td>
<td>homozygote</td>
<td>♀</td>
<td>decreased platelet cell number</td>
<td>Haematology test</td>
<td>WTSI</td>
<td>EuroPhenome</td>
<td>6.72E-12</td>
<td><img src="image7" alt="Crif3 Link" /></td>
</tr>
</tbody>
</table>
## CONNECT - Disease

### Filter your search

- Genes
- Phenotypes
- Diseases
  - Sources
    - OMIM
    - ORPHANET
    - DECIPHER
  - Classifications
    - With Curated Gene Associations
      - From human data (OMIM, Orphanet)
      - From mouse data (MGI)
    - With Predicted Gene Associations by Phenotype
      - From IMPC data
      - From IMPC data in linkage locus
      - From MGI data
      - From MGI data in linkage locus
  - Anatomy

### Search for: cardiac

Found 329 diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Source</th>
<th>Curated Genes</th>
<th>Candidate Genes by phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARDIOMYOPATHY, FAMILIAL RESTRICTIVE, 3, RCM3</td>
<td>OMIM</td>
<td>human</td>
<td></td>
</tr>
<tr>
<td>CARDIOMYOPATHY, FAMILIAL RESTRICTIVE, 1, RCM1</td>
<td>OMIM</td>
<td>human</td>
<td>MGI</td>
</tr>
<tr>
<td>CARDIOMYOPATHY, DILATED, JPP, CMD1FF</td>
<td>OMIM</td>
<td>human</td>
<td>MGI</td>
</tr>
<tr>
<td>CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 2, CMH2</td>
<td>OMIM</td>
<td>human</td>
<td>MGI</td>
</tr>
<tr>
<td>SUBAORTIC STENOSIS, MEMBRANOUS</td>
<td>OMIM</td>
<td>human</td>
<td>MGI</td>
</tr>
<tr>
<td>MILLER-DIEKER SYNDROME (MDS)</td>
<td>DECIPHER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CARDIAC ARRHYTHMIA, ANKYRIN-9-RELATED</td>
<td>OMIM</td>
<td>human</td>
<td>IMPC, MGI</td>
</tr>
</tbody>
</table>
CONNECT- Cross-species phenotype comparisons by semantic similarity

**Cross-species**

- **larynx**
  - UBERON:0001737
  - MA:0000414

- **abnormal**
  - PATO:000460
  - larynx morphology
    - MP:0002249

Abnormality of the larynx
HP:0001600

Abnormality of the voice
HP:0001608

Speech articulation difficulties
HP:0008088

Abnormal laryngeal cartilage morphology
MP:0002256

**Human Disease: PFEIFFER SYNDROME**

- Premature suture closure
- Maxilla hypoplasia
- Malocclusion
- Shortened head
- Ocular hypertelorism

**Cross-species Phenotype**

- Coronal craniosynostosis
  - HP:0004440

- Hypoplasia of the maxilla
  - HP:0000327

- Dental crowding
  - HP:0000678

- Brachyterunccephaly
  - HP:0000244

- Hypotelorism
  - HP:0000316

**Most similar mouse model:** CD1.Cg-Fgfr2tm4Lni/H

- Premature suture closure
- Short maxilla
- Malocclusion
- Shortened head
- Ocular hypertelorism

**IMPC**
## CONNECT - Disease

**Allele - Nbeal2<sup>tm1a(EUCOMM)Wtsi</sup>**

### Potential Disease Models

<table>
<thead>
<tr>
<th>Disease Name</th>
<th>Source</th>
<th>Disease Gene Ortholog</th>
<th>Syntenic Disease Locus</th>
<th>Mouse Literature Evidence (MGI)</th>
<th>MGI Mouse Phenotype Evidence (Phenodigm)</th>
<th>IMPC Mouse Phenotype Evidence (Phenodigm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray Platelet Syndrome</td>
<td>OMIM:139090</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>90.31</td>
<td>62.24</td>
</tr>
<tr>
<td>Gray Platelet Syndrome</td>
<td>ORPHANET:721</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet Signal Processing Defect</td>
<td>OMIM:173590</td>
<td></td>
<td></td>
<td></td>
<td>91.37</td>
<td>67.05</td>
</tr>
</tbody>
</table>
## Disease: Hermansky-Pudlak Syndrome

**Name**: Hermansky-Pudlak Syndrome 7  
**Synonyms**: -  
**Locus**: 6p22.3  
**Associated Human Genes**: Dtnbp1  
**Mouse Orthologs**: Dtnbp1  
**Source**: OMIM:614078

### Potential Mouse Models

<table>
<thead>
<tr>
<th>Mouse Gene Symbol</th>
<th>Disease Gene Ortholog</th>
<th>Syntenic Disease Locus</th>
<th>Mouse Literature Evidence (MGI)</th>
<th>MGI Mouse Phenotype Evidence (Phenodigm)</th>
<th>IMPC Mouse Phenotype Evidence (Phenodigm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dtnbp1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>78.96</td>
<td>66.52</td>
</tr>
<tr>
<td>Hps3</td>
<td></td>
<td></td>
<td></td>
<td>88.9</td>
<td></td>
</tr>
<tr>
<td>Tyr</td>
<td></td>
<td></td>
<td></td>
<td>87.95</td>
<td></td>
</tr>
</tbody>
</table>

**OMIM:614075 Disease**  
**Phenotype Terms**  
- Bruising susceptibility
- Albinism
- Ocular albinism
- Impaired platelet aggregation

**Associated Mouse Models (Phenodigm predicted)**  
- 78.96: Dtnbp1 (DD/GK)  
  - Diluted coat color
  - Abnormal eye pigmentation
  - Abnormal kidney physiology
  - Abnormal blood coagulation
  - Decreased platelet cell number
  - Abnormal platelet dense granule number
  - Decreased platelet serotonin level
  - Abnormal choroid morphology
  - Abnormal choroid pigmentation
  - Abnormal retinal pigment epithelium morphology
  - Abnormal platelet physiology
  - Decreased platelet aggregation

- 73.61: Dtnbp1 (DBA/2J)  
  - Diluted coat color
  - Decreased eye pigmentation
  - Increased bleeding time

- 66.52: Dtnbp1 (UHDD/187; B6)  
  - Increased circulating calcium level
  - Increased leukocyte cell number
  - Increased circulating phosphate level
  - Abnormal skin morphology
  - Abnormal coat/hair pigmentation
  - Abnormal iris pigmentation
  - Abnormal retinal pigmentation
  - Increased circulating cholesterol level
  - Decreased circulating serum albumin level
  - Decreased circulating glucose level
  - Decreased mean corpuscular hemoglobin concentration
**CONNECT-Disease gene discovery**

### Disease: Malignant Hyperthermia, Susceptibility To, 3

<table>
<thead>
<tr>
<th>Name</th>
<th>Malignant Hyperthermia, Susceptibility To, 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synonyms</td>
<td>MHS3</td>
</tr>
<tr>
<td>Locus</td>
<td>7q21-q22</td>
</tr>
<tr>
<td>Associated Human Genes</td>
<td>-</td>
</tr>
<tr>
<td>Mouse Orthologs</td>
<td>-</td>
</tr>
<tr>
<td>Source</td>
<td>OMIM:154276</td>
</tr>
</tbody>
</table>

**Phenotype Terms**
- Hypertonia
- Fever
- Malignant hyperthermia
- Hyperkalemia
- Hyperphosphatemia
- Lactic acidosis
- Myopathy
- Elevated serum creatine phosphokinase
- Viral infection-induced rhabdomyolysis
- Exercise-induced rhabdomyolysis
- Anesthetic-Induced rhabdomyolysis
- Alcohol-induced rhabdomyolysis
- Decreased blood urea nitrogen level
- Decreased circulating sodium level
- Increased circulating phosphate level
- Increased circulating chloride level
- Increased circulating bilirubin level
- Decreased neutrophil cell number
- Decreased body weight
- Decreased basophil cell number
- Decreased eosinophil cell number
- Decreased mean circulating potassium level
- Decreased mean platelet volume

### Potential Mouse Models

<table>
<thead>
<tr>
<th>Mouse Gene Symbol</th>
<th>Disease Gene Ortholog</th>
<th>Syntenic Disease Locus</th>
<th>Mouse Literature Evidence (MGI)</th>
<th>MGI Mouse Phenotype Evidence (Phenodigm)</th>
<th>IMPC Mouse Phenotype Evidence (Phenodigm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gpr22</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gpc2</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CONNECT-Data download
CONNECT - RESTFUL API

https://github.com/mpi2/PhenotypeArchive/wiki/REST-APIS

The IMPC offers the following RESTful APIs for consuming data:

Genotype-Phenotype API
Please see the Genotype-Phenotype API documentation

Experimental observation API
Please see the Experimental observation API documentation

Statistical results API
Please see the Statistical results API documentation
CONNECT- Gene-Phenotype API

Genotype associated phenotype calls
There are many ways to get information about the MP terms associated to the different KO genes. You can select data per:

- phenotyping center (UCD, Wellcome Trust Sanger Institute, JAX, etc.)
- phenotyping program (legacy MGP, EUMODIC, etc.)
- phenotyping resource (EuroPhenome, MGP, IMPC)
- phenotyping pipeline (EUMODIC1, EUMODIC2, MGP, IMPC adult, IMPC embryonic, etc.)
- phenotyping procedure or parameter
- allele name or MGI allele ID
- strain name or MGI strain ID
- gene symbol or MGI gene ID
- or a combination of all these fields

Retrieve all genotype-phenotype associations for a specific MP term
We will constrain the results by adding a condition to the q (query) parameter using the specific mp_term_name field. To retrieve genotype associated to "decreased total body fat amount", simply specify q=mp_term_name:"decreased total body fat amount"

```
curl
   --basic
   -X GET
   "http://www.ebi.ac.uk/mi/impc/solr/genotype-phenotype/select?q=mp_term_name:"decreased total body fat amount"
```
CONNECT- Experimental data & Stats API

- There are many ways to select and filter
- all data points for a parameter
- all data points for a gene for one experiment
- all data for a specific pipeline
- all stats results below a pvalue
- all stats results with sexual dimorphism
Disseminate statistical results - API

API documentation: [https://github.com/mpi2/PhenotypeArchive/wiki/REST-APIs](https://github.com/mpi2/PhenotypeArchive/wiki/REST-APIs)

```xml
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  <double name="intercept_estimate">5.752570152282715</double>
  <double name="group_2_residuals_normality_test">0.613598015499115</double>
  <double name="genotype_effect_stder_estimate">0.3152709901332855</double>
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  <str name="doc_id">ESLIM_009_001_703_1</str>
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  <str name="group_2_genotype">HEPD0528_4_A08</str>
</doc>
```
Lets Explore

• Try searching for your favourite gene
• Now try favorite phenotype
• Disease