

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

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Part of the MPI2 consortium

[www.mousephenotype.org](http://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)**



# Background: Building on IKMC Success

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



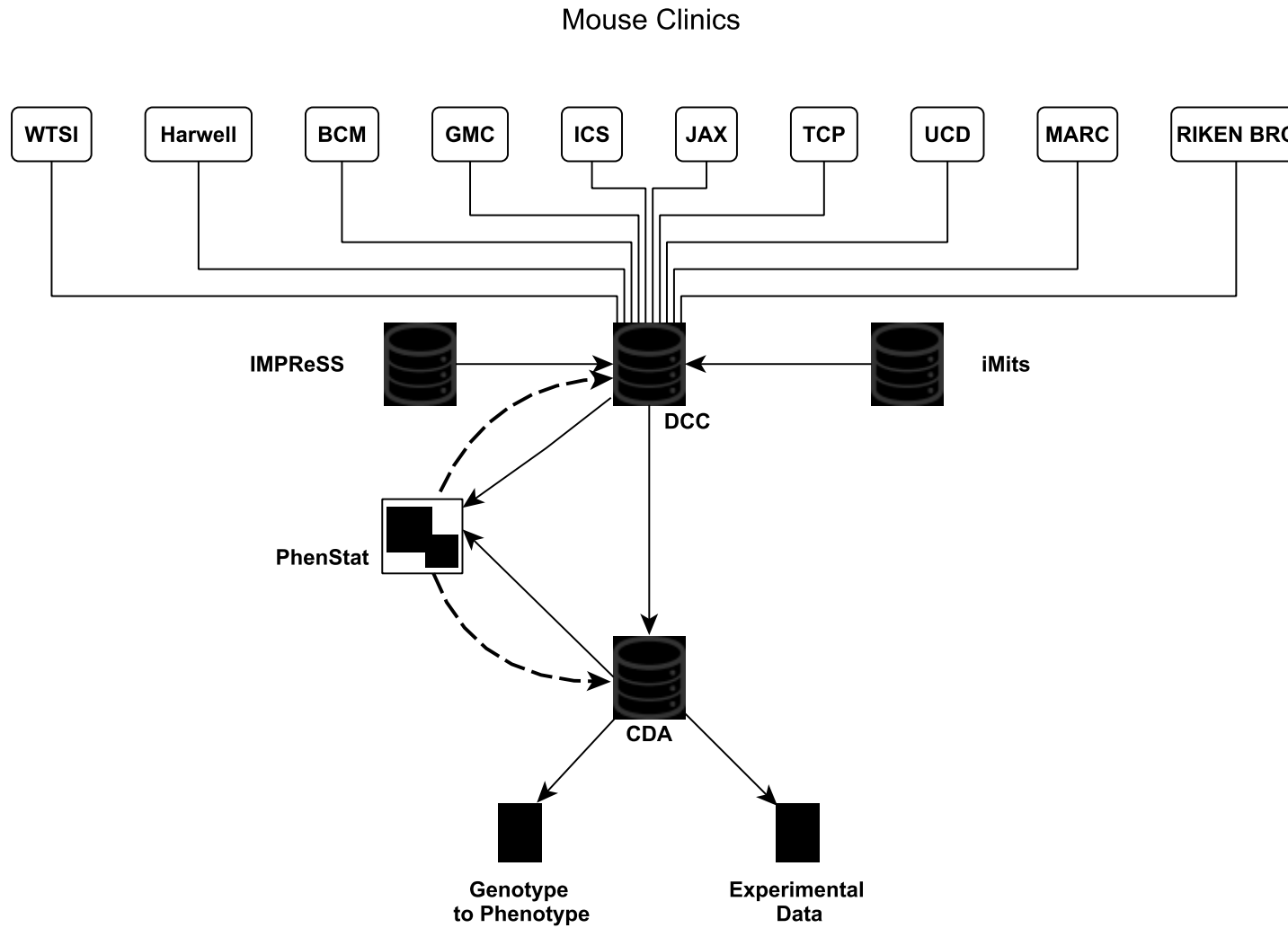
# Background: The IMPC

International Mouse Phenotype Consortium

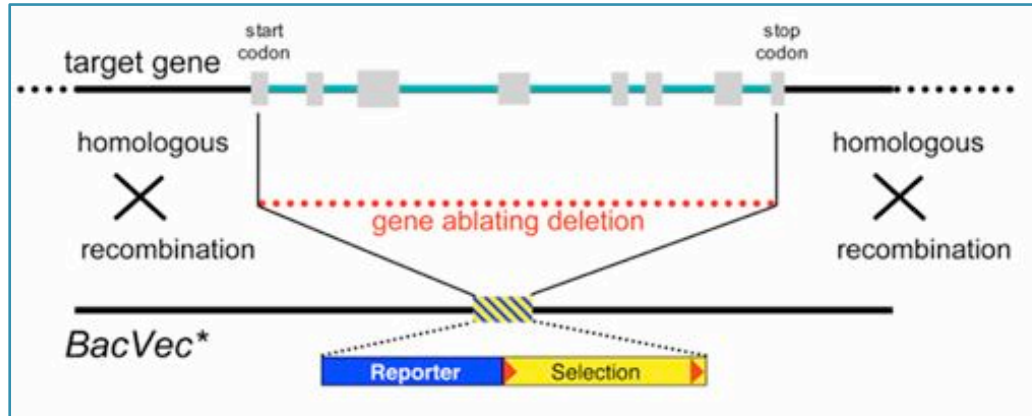
- Create and Characterize 20,000 knockout lines over 10 years
- Phase 1- 5000 strains by 2016
- Publish & Annotate Data in near Real-Time
- Integrate IMPC data with human mutation and disease repositories



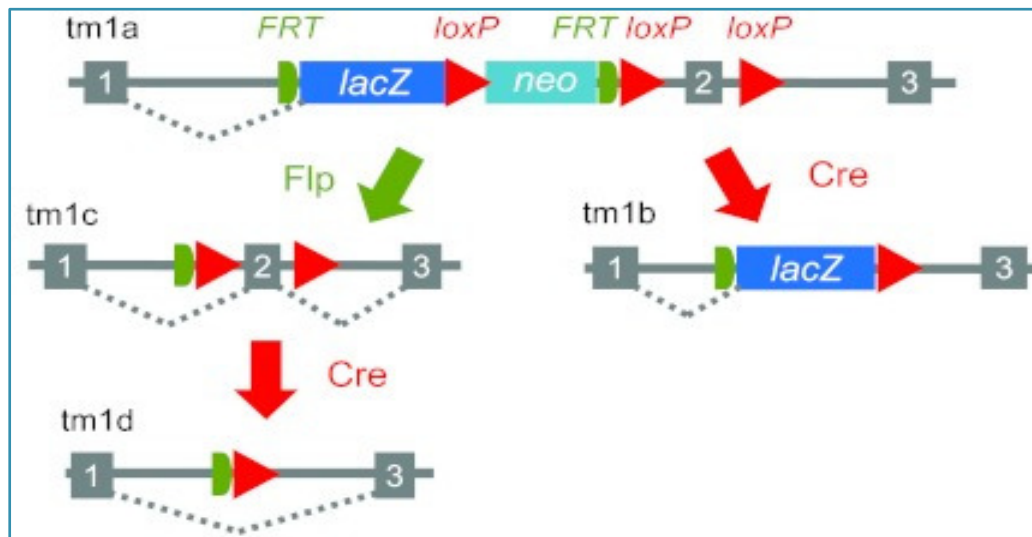
# CHARACTERIZE- High quality data



# CREATE: Knockout Line Production



KOMP  
Velicogene



EUCOMM

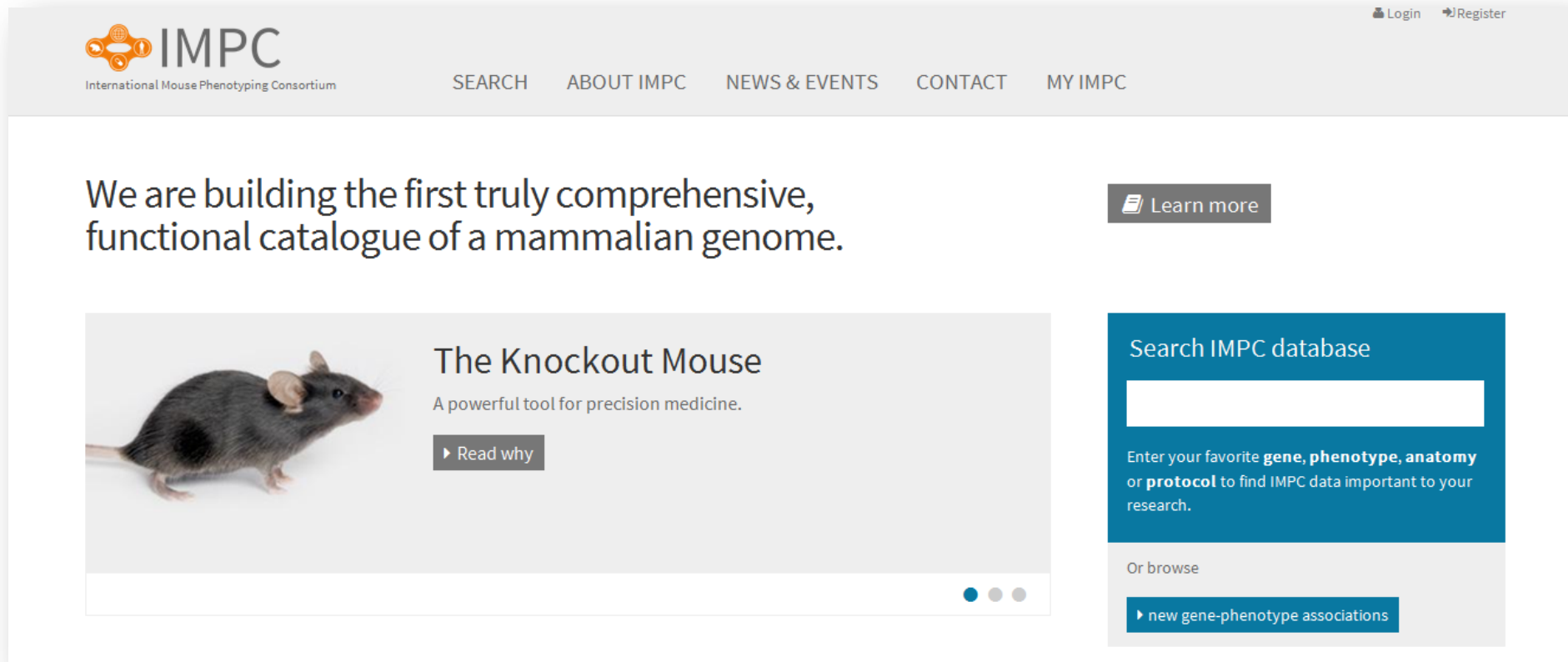


# DEMO I





# Home page




The screenshot shows the IMPC website home page. At the top left is the IMPC logo with the text "International Mouse Phenotyping Consortium". To the right are navigation links: "SEARCH", "ABOUT IMPC", "NEWS & EVENTS", "CONTACT", and "MY IMPC". In the top right corner, there are "Login" and "Register" links. The main content area features a large heading: "We are building the first truly comprehensive, functional catalogue of a mammalian genome." Below this is a "Learn more" button. A featured section titled "The Knockout Mouse" includes an image of a mouse and the text "A powerful tool for precision medicine." with a "Read why" button. On the right side, there is a search box titled "Search IMPC database" with a text input field and instructions: "Enter your favorite gene, phenotype, anatomy or protocol to find IMPC data important to your research." Below the search box is a "Or browse" section with a "new gene-phenotype associations" button.

[mousephenotype.org](http://mousephenotype.org)



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



## The Knockout Mouse

A powerful tool for precision medicine.

[Read why](#)

## 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 scientific 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 by this web portal and by several data download features.

### 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](#)

### Rare Disease Models

Find mouse models of rare disease by either shared gene or shared phenotype features.

[Visit Disease Models](#)

### IMPreSS



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](#)

# CREATE: Knockout Line Production



IMPC Mouse Production

iMits website reports real-time production status

Home

Gene Summary

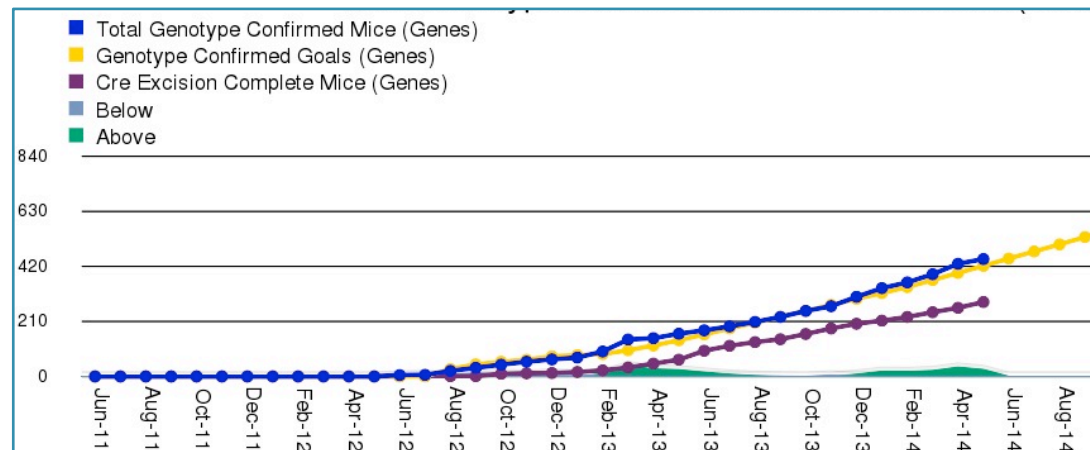
Mouse Production

Phenotyping

Contacts for Production Centres

Download of all Production


Status	Current Total (up to and inc. May)	Last Complete Month (May)
All genes	<a href="#">1379</a>	<a href="#">55</a>
ES Cell QC (genes)	<a href="#">877</a>	<a href="#">26</a>
ES QC Confirmed (genes)	<a href="#">795</a>	<a href="#">26</a>
ES QC Failed (genes)	<a href="#">22</a>	
Microinjections (genes)	<a href="#">831</a>	<a href="#">27</a>



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.



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[Read why](#)

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### iMITS

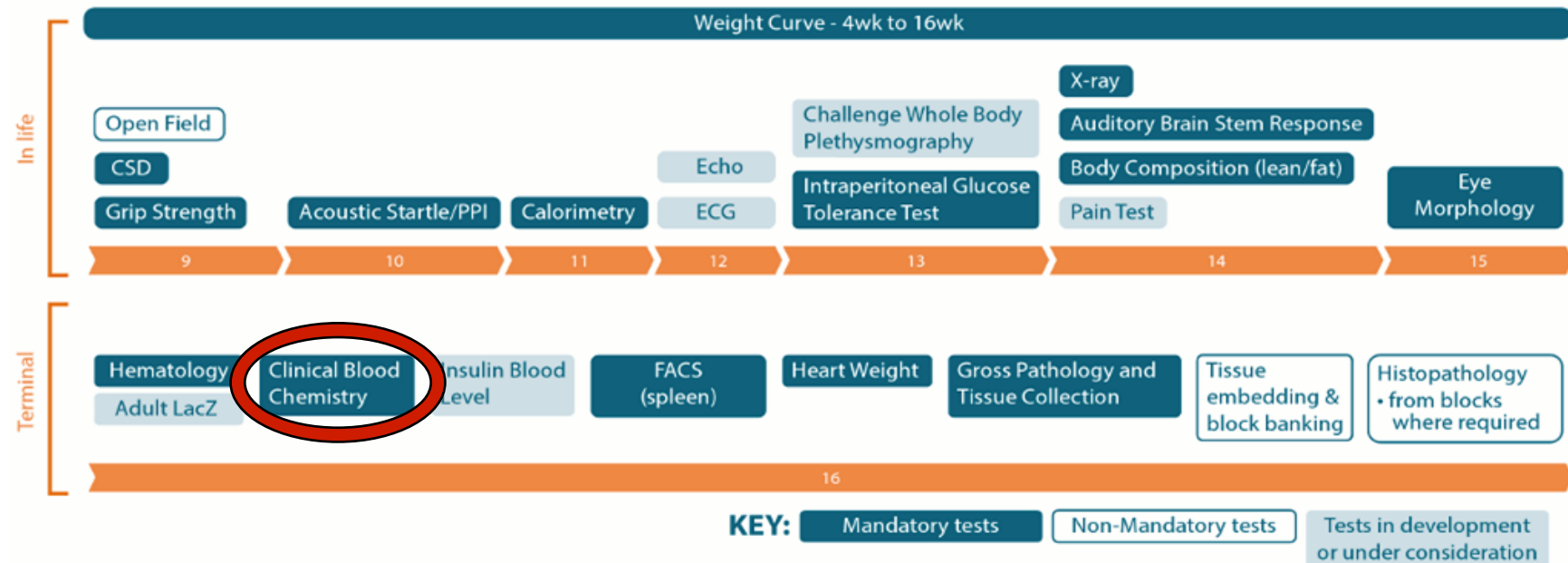
iMITS is the designated planning and tracking resource for IMPC mutant mouse strain production.

[Visit iMITS](#)

# CHARACTERIZE Adult phenotypes



7M + 7F Mutant Adult Mice



- [IMPReSS](#): (International Mouse Phenotyping Resource of Standardised Screens)
- Ascribe Biological Function to Each Gene
- Collaborate with phenotyping specialists

# Characterize

- Protocol

Clinical Blood Chemistry [IMPC\_CBC\_003] [View as PDF](#) / [Display Ontologies](#) / [Example XML Submission](#) / [Change History](#)

Purpose Experimental Design Equipment Procedure Notes Parameters Metadata

**Purpose**

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

Ontological description: MP:0001545 – blood physiology abnormalities.

**Experimental Design**

Minimum number of mutant animals: must maintain ≥ 7 size for male and female.

Age of animals: 16 weeks

Sexual dimorphism: Yes for some of the parameters.

- Data Parameter

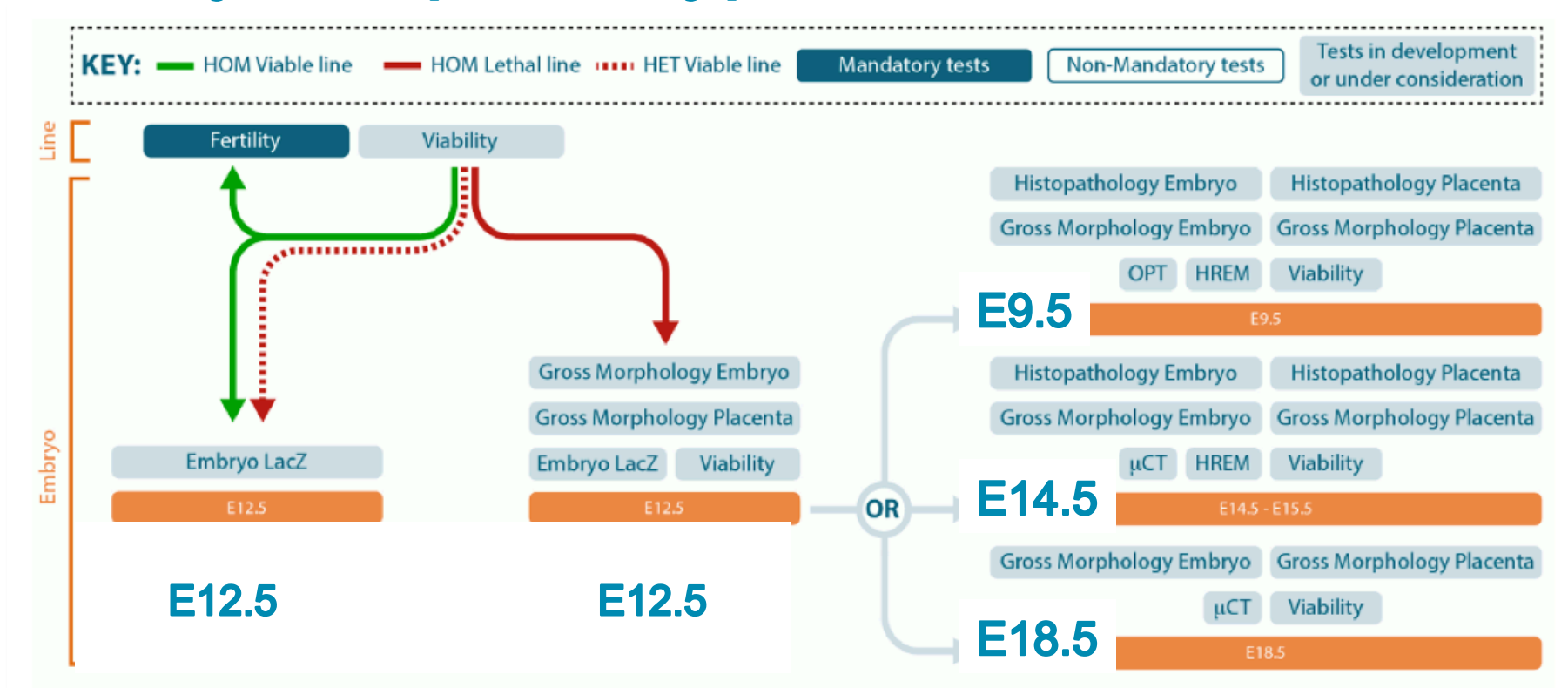
Parameter	Version	Type	Req. Upload	Req. Analysis	Annotation	Increment	Option	Ontology Options	Derived	Unit	Data Type
<a href="#">Sodium IMPC_CBC_001_001</a>	1.3	simpleParameter			✓					mmol/l	FLOAT
<a href="#">Potassium IMPC_CBC_002_001</a>	1.3	simpleParameter			✓					mmol/l	FLOAT
<a href="#">Chloride IMPC_CBC_003_001</a>	1.4	simpleParameter			✓					mmol/l	FLOAT
<a href="#">Urea (Blood Urea Nitrogen - BUN) IMPC_CBC_004_001</a>	1.5	simpleParameter	✓		✓					mg/dl	FLOAT

- Ontology



Parameter: Sodium IMPC_CBC_001_001					
	Option	Increment	Ontology Term	Ontology ID	Sex
INCREASED			increased circulating sodium level	<a href="#">MP:0005633</a>	
DECREASED			decreased circulating sodium level	<a href="#">MP:0005634</a>	
ABNORMAL			abnormal circulating sodium level	<a href="#">MP:0001776</a>	

# CHARACTERIZE Embryonic phenotypes



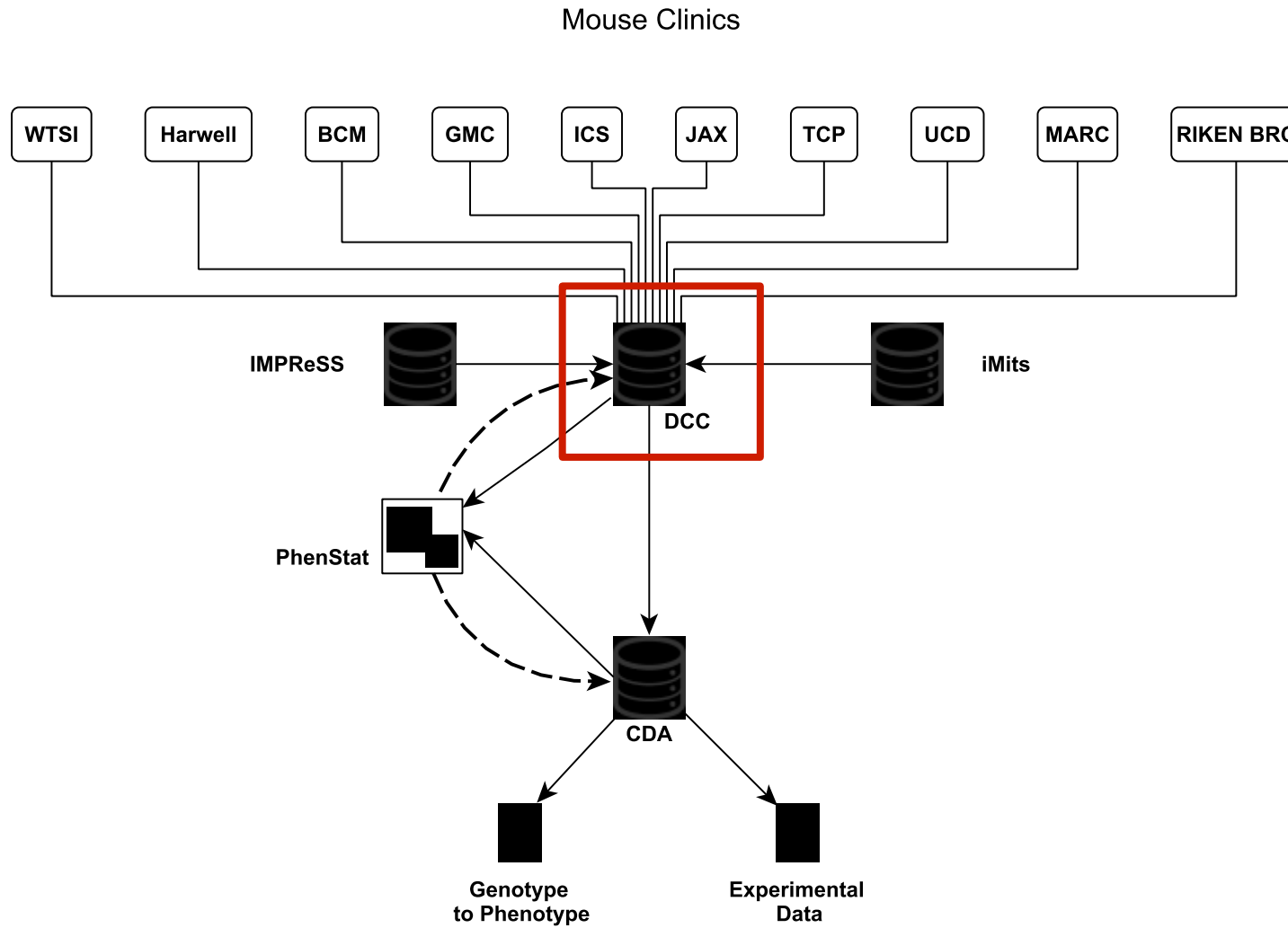
- A third of lines will be embryonic lethal
- Specialized pipeline created
- Cutting-edge imaging technologies being employed

# 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

**phenodcc** REPORTING TRACKER IMPRESS HELP BOOKMARK Terry Meehan sign out

View phenotype data Summary of data and QC issues Baylor College of Medicine - IMPC Pipeline - 1110001J03Rik EPO0647\_2\_B09 - 1110001J03Rik

Centre: **Baylor College of Medicine**  
Pipeline: **IMPC Pipeline**

Genes and Strains: **Procedures and Parameters**

IMPC ID	Status	Name	Count
IMPC_AL2_001	⊗	Adult LacZ	0
IMPC_ABR_001	⊗	Auditory Brain Stem Response	0
IMPC_ABR_002	✓	Auditory Brain Stem Response	0
IMPC_OXA_001	✓	Body Composition (DEXA lean/...	0
IMPC_BWT_001	✓	Body Weight	0
IMPC_CHI_001	⊗	Challenge Whole Body Plethys...	0
IMPC_CBC_001	⊗	Clinical Blood Chemistry	0
<b>IMPC_CBC_002</b>	✓	<b>Clinical Blood Chemistry</b>	0
IMPC_CBC_003	⊗	Clinical Blood Chemistry	0
IMPC_CSD_001	⬢	Combined S-HiRPA and Dysmor...	0

Parameters

IMPC ID	Status	Name	Count
IMPC_CBC_013_001	✓	Alanine aminotransferase	0
IMPC_CBC_007_001	✓	Albumin	0
IMPC_CBC_014_001	✓	Alkaline phosphatase	0
IMPC_CBC_003_001	⊗	Alpha-amylase	0
IMPC_CBC_012_001	✓	Aspartate aminotransfer...	0
IMPC_CBC_032_001	⊗	C-reactive protein	0
IMPC_CBC_009_001	⊗	Calcium	0
IMPC_CBC_003_001	✓	Chloride	0
IMPC_CBC_008_001	⊗	Creatine kinase	0
IMPC_CBC_005_001	✓	Creatinine (enzymatic m...	0

Gene details

id: MGI:1913367  
Symbol: 1110001J03Rik  
Genotype: 1110001J03Rik EPO0647\_2\_B09  
Strain: C57BL/6N  
Allele: 1110001J03Rik

**Clinical Blood Chemistry Alanine aminotransferase (U/l)**

Specimens and Quality Control Issues

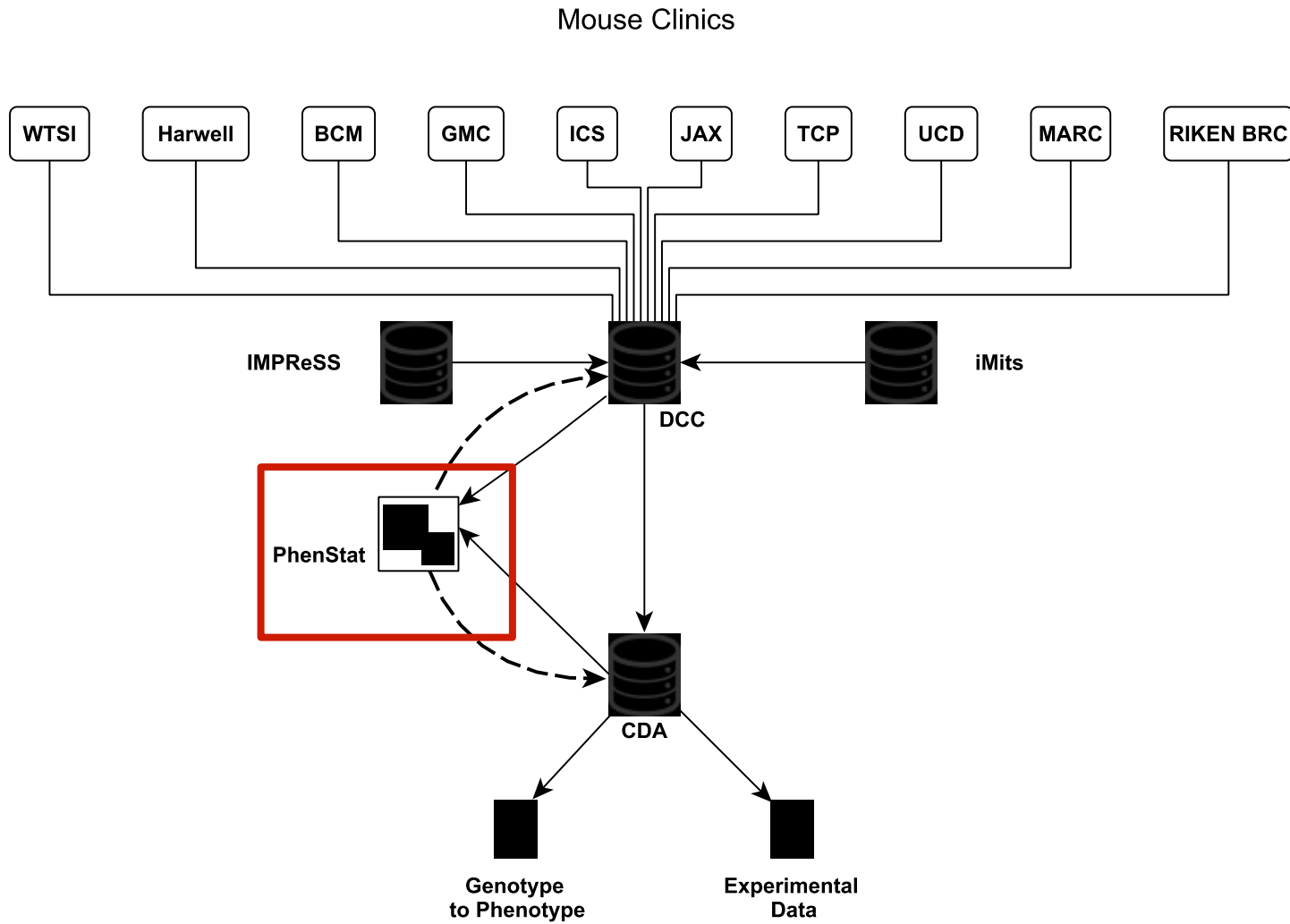
Quality Control issues: Specimen and experiment details Metadata details History

List of issues for current context

Title	Priority	Status	Raised By	Last update
Current data context does not have any Quality Control issues				



# CHARACTERIZE- STATS Analysis



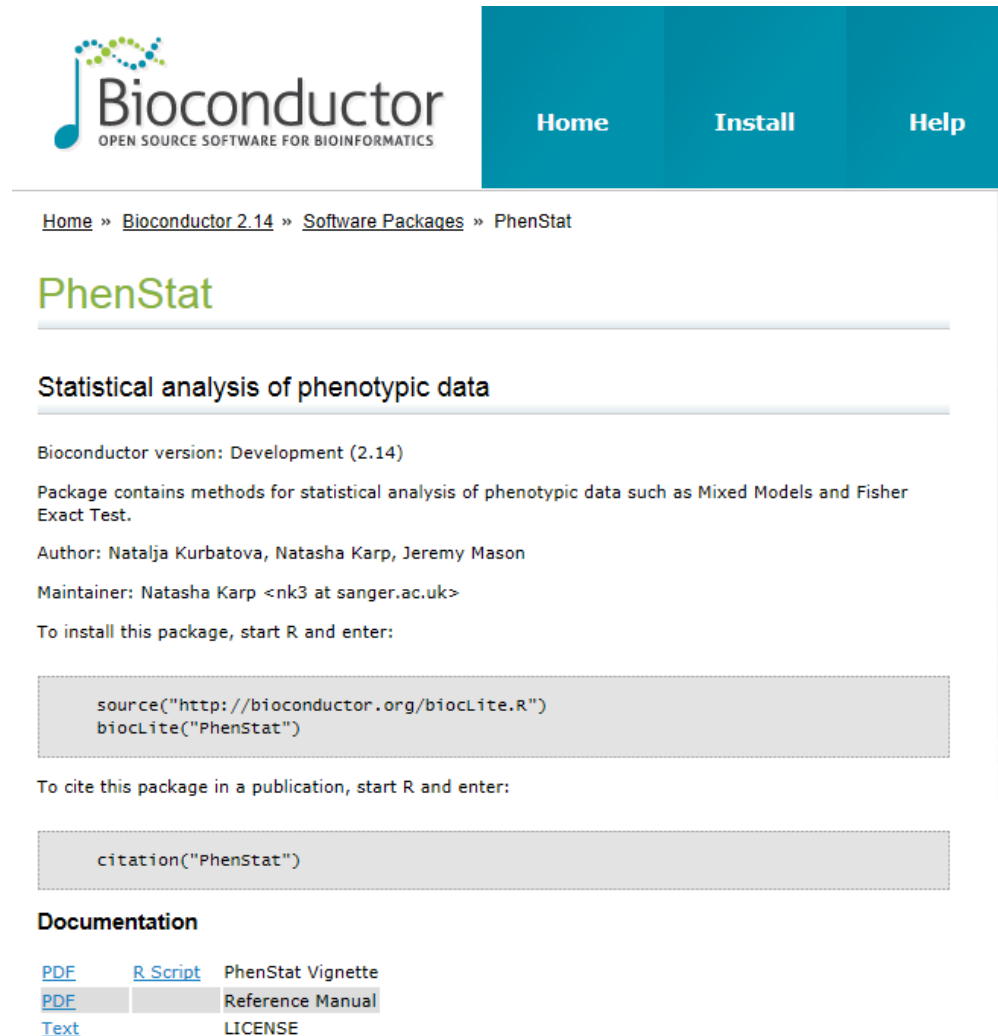
# CHARACTERIZE- PhenStat

## 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



The screenshot shows the Bioconductor website interface for the PhenStat package. At the top, the Bioconductor logo is displayed with the tagline "OPEN SOURCE SOFTWARE FOR BIOINFORMATICS". To the right, there are navigation buttons for "Home", "Install", and "Help". Below the navigation bar, the breadcrumb trail reads "Home » Bioconductor 2.14 » Software Packages » PhenStat". The main heading "PhenStat" is in green. Underneath, the title "Statistical analysis of phenotypic data" is followed by a horizontal line. The page content includes: "Bioconductor version: Development (2.14)", "Package contains methods for statistical analysis of phenotypic data such as Mixed Models and Fisher Exact Test.", "Author: Natalja Kurbatova, Natasha Karp, Jeremy Mason", "Maintainer: Natasha Karp <nk3 at sanger.ac.uk>", and "To install this package, start R and enter:". Below this is a code block containing the installation command: 

```
source("http://bioconductor.org/biocLite.R")
biocLite("PhenStat")
```

 Following this, it says "To cite this package in a publication, start R and enter:" and provides another code block: 

```
citation("PhenStat")
```

 At the bottom, there is a "Documentation" section with links for "PDF", "R Script", "PhenStat Vignette", "PDF", "Reference Manual", "Text", and "LICENSE".



# 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*



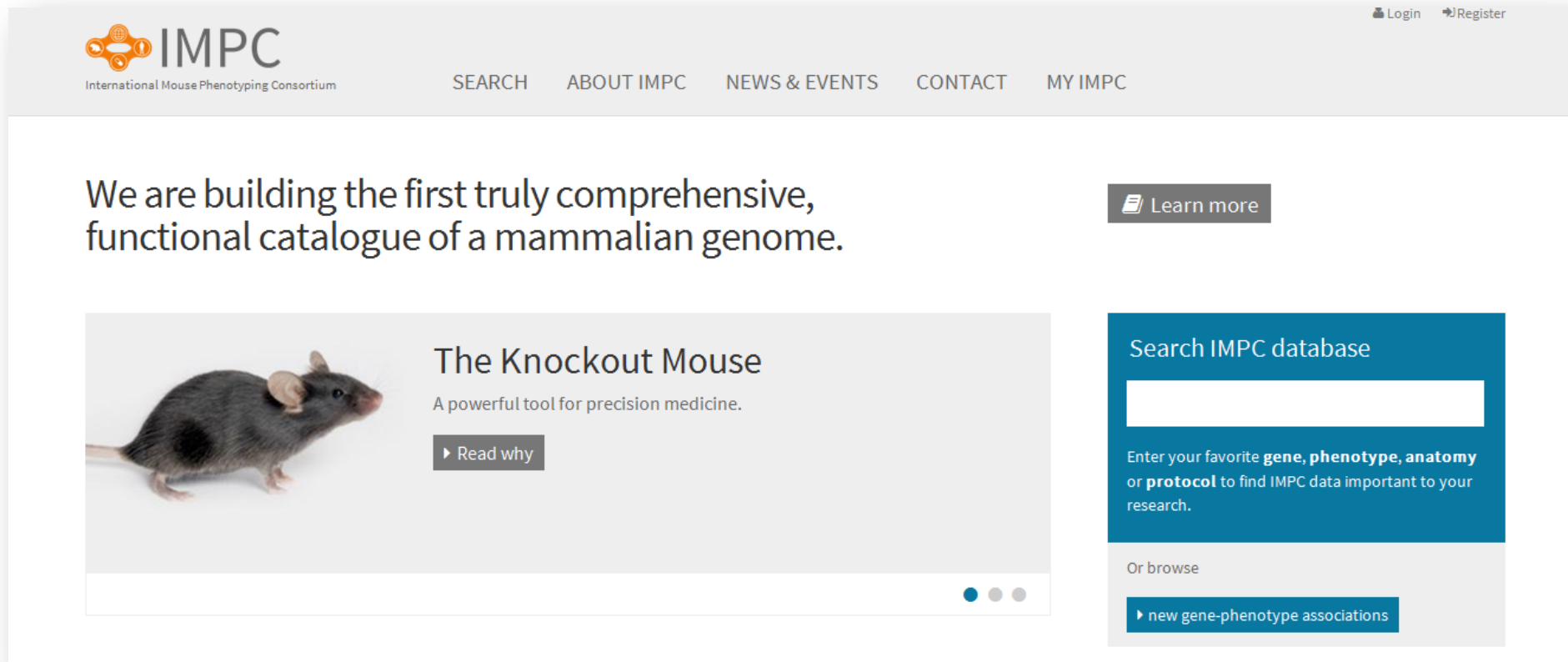
# CHARACTERIZE- Other Approaches (BAYESIAN) II

- 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



# Home page



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[mousephenotype.org](http://mousephenotype.org)

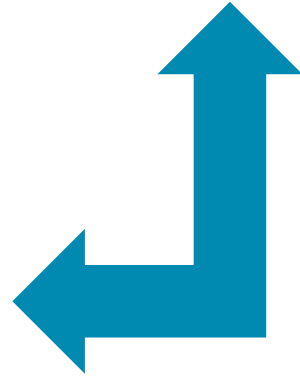


# CATALOGUE

Found 288 genes [View example search](#) [Download](#)

Gene	Production Status	Phenotype Status	
<b>Smyd5</b>	ES cells Mice	phenotype data available	<a href="#">Interest</a>
<b>Apol7a</b>	ES cells Mice	phenotype data available	<a href="#">Interest</a>
<b>Slc38a10</b>	ES cells Mice	phenotype data available	<a href="#">Interest</a>
<b>Xbp1</b>	ES cells Mice	phenotype data available	<a href="#">Interest</a>

Follow genes you are interested in  
IMPC will send an email when new data is published



# CONNECT

## 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 for a specific gene, type of gene, phenotype, procedure or phrase

# CONNECT- Search

Home » Search

### Filter your search

[?](#)

- ▶ Genes 22
- ▼ Phenotypes 23
  - adipose tissue 0
  - behavior/neurological 0
  - cardiovascular system 0
  - craniofacial 0
  - embryogenesis 0
  - endocrine/exocrine gland 0
  - growth/size/body 3
  - hearing/vestibular/ear 0
  - hematopoietic system 0
  - homeostasis/metabolism 20
  - immune system 0
  - integument 0
  - limbs/digits/tail 0
  - mortality/aging 0


[View example search](#)

Found 23 phenotypes [Download](#)

Phenotype	Definition
<a href="#">decreased circulating glucose level</a>	less than the normal concentration in the blood of this major monosaccharide of the body; it is an important energy source
<a href="#">abnormal glucose homeostasis</a>	anomaly in the processes involved in the maintenance of an internal equilibrium of <b>glucose</b> in the fluids and tissues
<a href="#">abnormal circulating glucose level</a>	any anomaly in the concentration in the blood of the major monosaccharide of the body

# CONNECT- Filter

Filter your search



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

Filter by phenotype, source, or pathology.

Filter your search

Gene

- ✕ Phenotyping Complete

Phenotype

- ✕ hematopoietic system

Disease

- ✕ From human data (OMIM, Orphanet)

[✕ Remove all facet filters](#)

Found 22 genes

# CONNECT- Gene page

## Gene: Nbeal2

Name neurobeachin-like 2  
MGI Id [MGI:2448554](#)

[Login to register interest](#)

Status

ES cells

Mice  
tm1a

Mice  
tm1e

phenotype data available

[Order](#)

ENSEMBL Links [Gene View](#) [Location View](#) [Compara View](#)

[Gene Browser](#) [ENU\(27\)](#)

Gene Summary at top of page



# CONNECT- Gene to phenotype

## 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

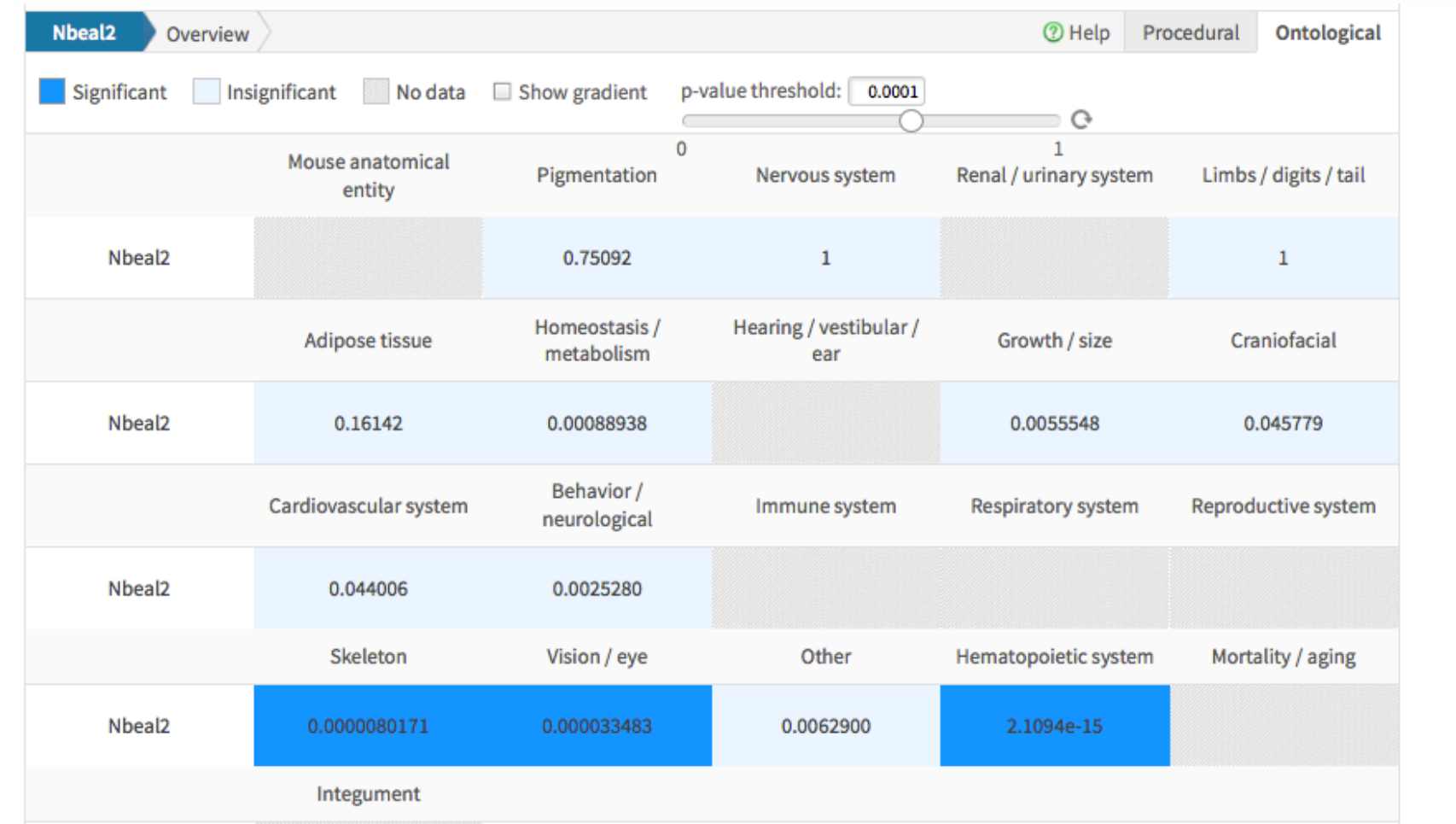
- [immune system phenotype](#). Evidence from IMPC (1)



skeleton phenotype

Phenotype overview

# CONNECT- Gene to phenotype



Phenotype heatmap





# CONNECT- Gene to phenotype

▶ Top level MP: All

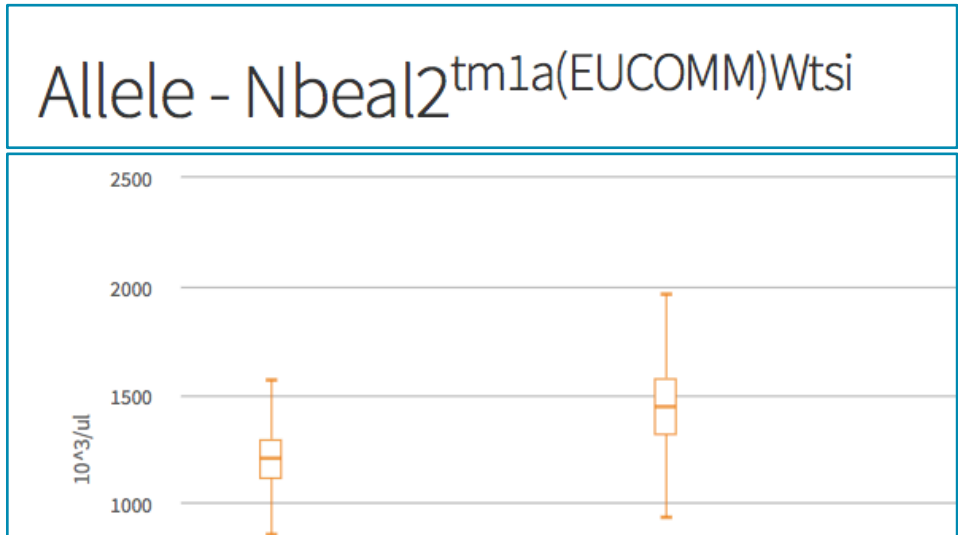
▶ Source: All

Drill down further for detailed phenotype data

Total number of results: 8

Phenotype	Allele	Zygoty	Sex	Procedure   Parameter	Phenotyping Center	Source	P Value	Graph
<a href="#">increased mean platelet volume</a>	<a href="#">Nbeal2<sup>tm1a(EUCOMM)Wtsi</sup></a>	homozygote	♀ ♂	Hematology   Mean platelet volume	WTSI	IMPC	0.0	
<a href="#">decreased platelet cell number</a>	<a href="#">Nbeal2<sup>tm1a(EUCOMM)Wtsi</sup></a>	homozygote	♀ ♂	Hematology   Platelet count	WTSI	IMPC	2.11E-15	
<a href="#">increased leukocyte cell number</a>	<a href="#">Nbeal2<sup>tm1a(EUCOMM)Wtsi</sup></a>	homozygote	♂	Hematology   White blood cell count	WTSI	IMPC	4.71E-8	
<a href="#">decreased bone mineral density</a>	<a href="#">Nbeal2<sup>tm1a(EUCOMM)Wtsi</sup></a>	homozygote	♀ ♂	Body Composition (DEXA lean/fat)   Bone Mineral Density (excluding skull)	WTSI	IMPC	4.18E-6	

# CONNECT- Display of data

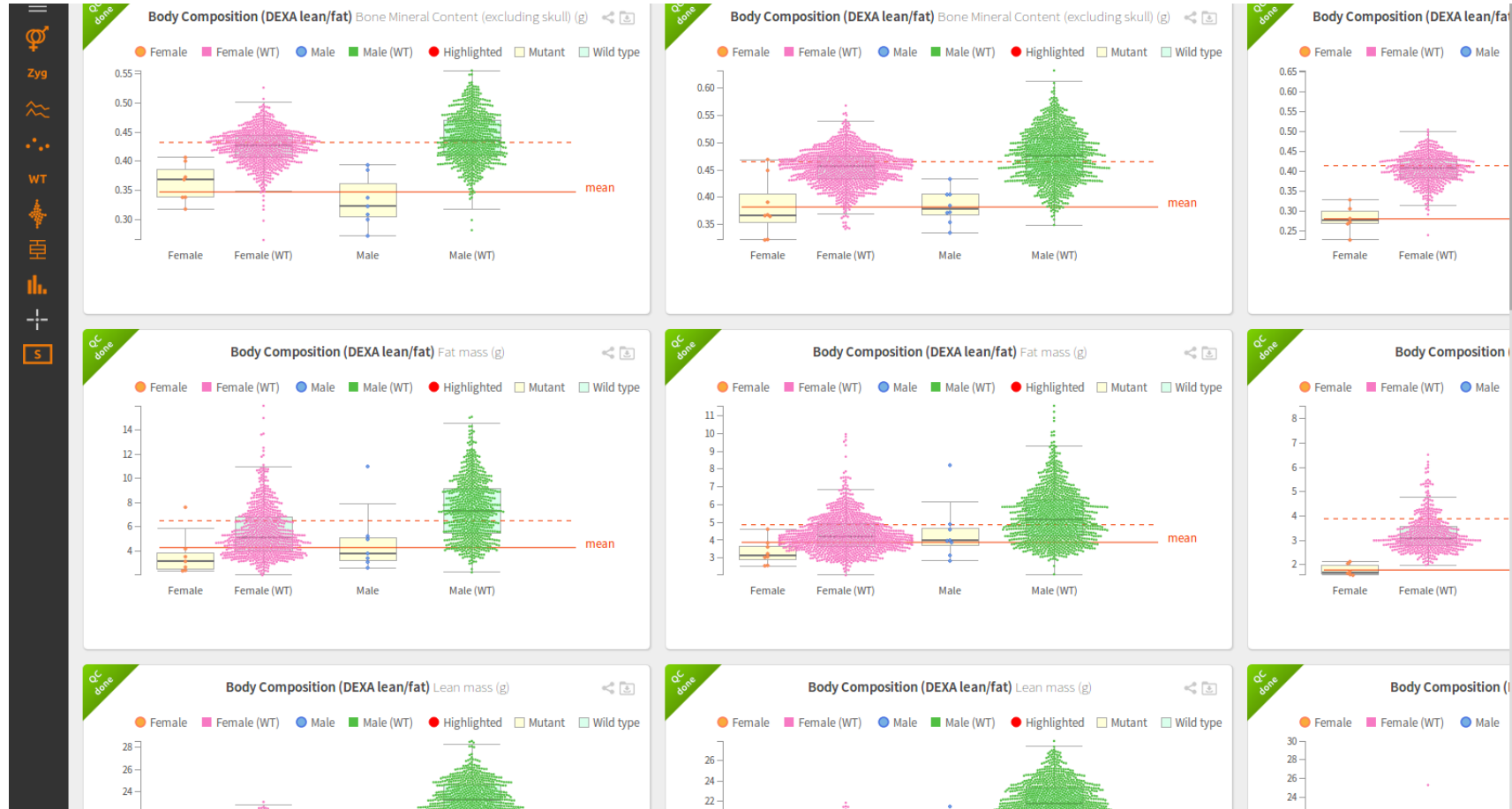


P Value	Classification			
2.1094E-15	Different effect size, males greater			
	Sex	Sex*Genotype P Value	Effect size	Standard Error
	Female	7.1758E-22	-534.08	± 54.458
	Male	9.1166E-38	-737.84	± 55.404

# CONNECT- Data in near real time

Phenotype	Allele	Zygoty	Sex	Procedure   Parameter	Phenotyping Center	Source	P Value	Graph
<a href="#">abnormal bone structure</a>	<a href="#">Dnase1l2<sup>tm1.1(KOMP)Wtsi</sup></a>	heterozygote	♀ ♂	Body Composition (DEXA lean/fat)   Bone Area (BMC/BMD)	JAX	IMPC	0.0	
<a href="#">abnormal bone structure</a>	<a href="#">Dnase1l2<sup>tm1.1(KOMP)Wtsi</sup></a>	heterozygote	♀ ♂	Body Composition (DEXA lean/fat)   Bone Area (BMC/BMD)	UC Davis	IMPC	0.0	
<a href="#">decreased body length</a>	<a href="#">Dnase1l2<sup>tm1.1(KOMP)Wtsi</sup></a>	heterozygote	♀ ♂	Body Composition (DEXA lean/fat)   Body length	UC Davis	IMPC	0.0	
<a href="#">decreased body weight</a>	<a href="#">Dnase1l2<sup>tm1.1(KOMP)Wtsi</sup></a>	homozygote	♀ ♂	Grip Strength   Body weight	MRC Harwell	IMPC	0.0	

# Pheno-DCC- Pre QC view



# X-Ray Images Lateral

phenoview REPORTING TRACKER QUALITY CONTROL IMPRESS HELP BOOKMARK Not logged in | sign in

Exit viewer H • C57BL/6NTac • Mapkbp1<sup>tm1b/(UCOMM)Hmsu</sup> • X-ray • XRay Images Lateral Orientation

WILDTYPE MUTANT

Zoom: 10 Brightness: -1 Contrast: 0 Invert colour  Red  Green  Blue

Zoom: 10 Brightness: -1 Contrast: 0 Invert colour  Red  Green  Blue

Name: ADHS-TM1B-IC/12.1a_5342318 Date: 20 May 2013, Monday Sex: Female (wildtype) Zygosity: Homozygous	Name: ADHS-TM1B-IC/12.1d_5342321 Date: 20 May 2013, Monday Sex: Male (wildtype) Zygosity: Homozygous	Name: ADHS-TM1B-IC/12.2d_5343459 Date: 20 May 2013, Tuesday Sex: Male (wildtype) Zygosity: Homozygous	Name: MAPKBP1-TM1B-IC/5.1d_5106365 Date: 10 April 2013, Wednesday Sex: Male (mutant) Zygosity: Homozygous	Name: MAPKBP1-TM1B-IC/5.1i_5106370 Date: 10 April 2013, Wednesday Sex: Male (mutant) Zygosity: Homozygous	Name: MAPKBP1-TM1B-IC/5.3d_5209721 Date: 8 April 2013, Monday Sex: Male (mutant) Zygosity: Homozygous
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# LacZ Images

phenoview REPORTING TRACKER QUALITY CONTROL IMPRESS HELP BOOKMARK Hugh Morgan | [sign out](#)

Exit viewer H • C57BL/6NTac • Clstn3<sup>tm1b(EUCOMM)Hmgu</sup> • Adult LacZ • LacZ Images Wholemount

Name: CLSTN3-TM1B-IC/7.1b\_5289960  
Date: 31 March 2014, Monday  
Sex: Female (mutant)  
Zygosity: Heterozygous

Zoom: 10  100  
Brightness: -1  1  
Contrast: 0  3  
 Invert colour  Red  Green  Blue

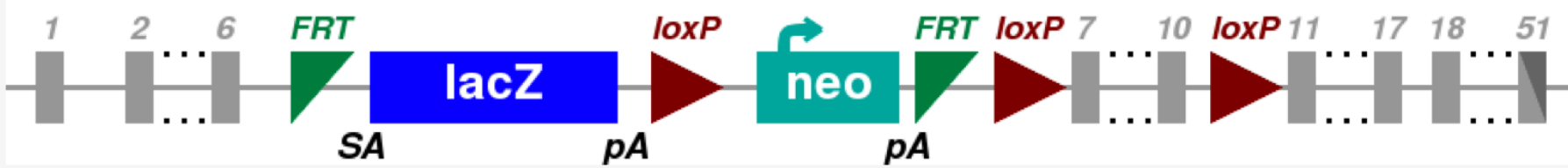
Name: CLSTN3-TM1B-IC/7.1b\_5289960  
Date: 31 March 2014, Monday  
Sex: Female (mutant)  
Zygosity: Heterozygous

Name: CRELD2-TM1B/8.1a\_5087721  
Date: 10 November 2012, Saturday  
Sex: Female (wildtype)  
Zygosity: Homozygous



# CONNECT- Find resources

Order Mice & ES Cells directly from website

Product Type	Strain of	MGI Allele Name	Allele	Product	Order /
 <p><a href="#">Download this image in high resolution</a> <a href="#">Download this image</a></p>					



# CONNECT- Disease

Filter your search

- ▶ Genes 15
- ▶ Phenotypes 2
- ▼ Diseases 329
  - ▼ Sources
    - OMIM 262
    - ORPHANET 62
    - DECIPHER 5
  - ▶ Classifications
  - ▼ With Curated Gene Associations
    - From human data (OMIM, Orphanet) 212
    - From mouse data (MGI) 81
  - ▼ With Predicted Gene Associations by Phenotype
    - From IMPC data 41
    - From IMPC data in linkage locus 1
    - From MGI data 261
    - From MGI data in linkage locus 35
- ▶ Anatomy 0

cardiac

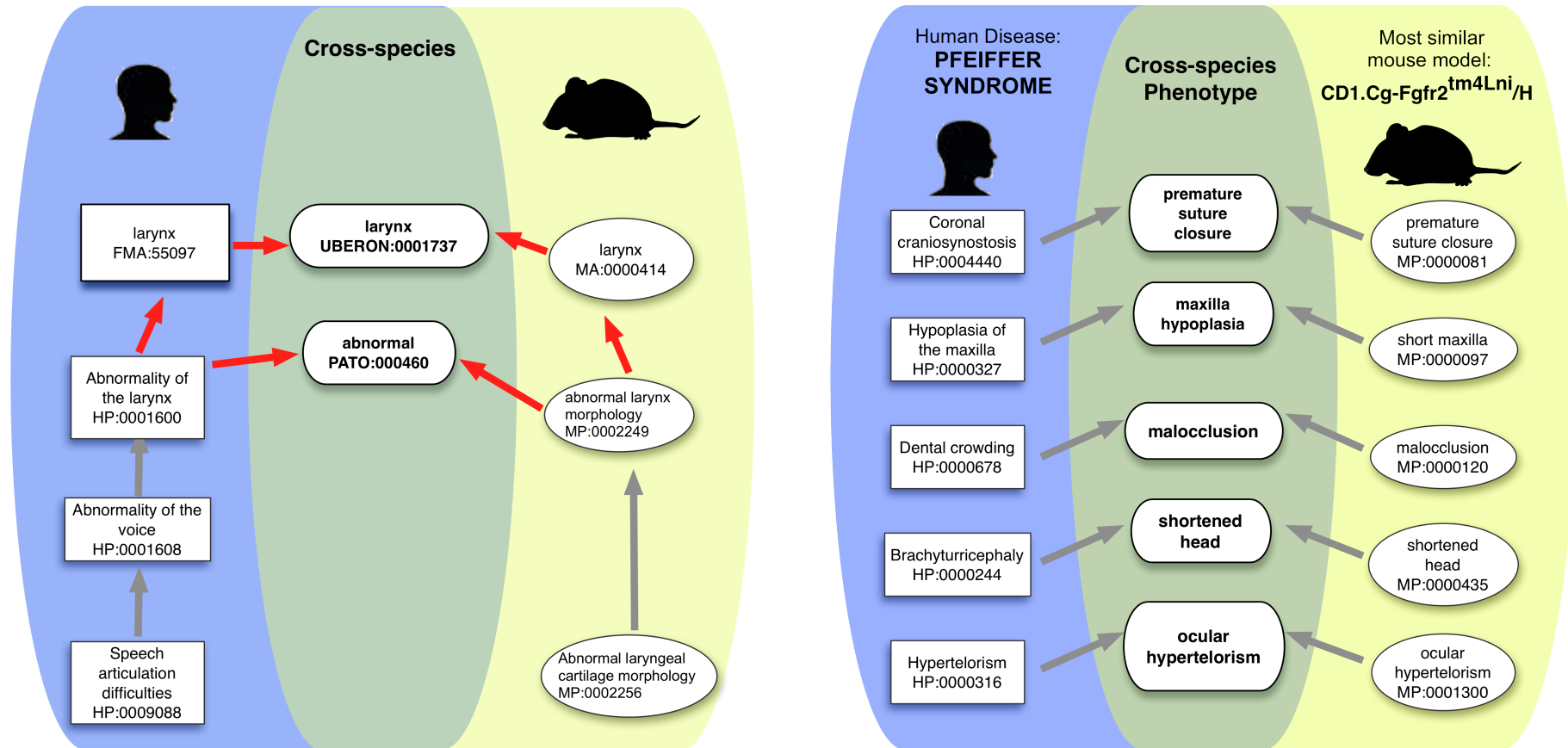
View example search

Found 329 diseases Download

Disease	Source	Curated Genes	Candidate Genes by phenotype
<a href="#">CARDIOMYOPATHY, FAMILIAL RESTRICTIVE, 3; RCM3</a>	OMIM	human	
<a href="#">CARDIOMYOPATHY, FAMILIAL RESTRICTIVE, 1; RCM1</a>	OMIM	human	MGI
<a href="#">CARDIOMYOPATHY, DILATED, 1FF; CMD1FF</a>	OMIM	human	MGI
<a href="#">CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 2; CMH2</a>	OMIM	human	MGI
<a href="#">SUBAORTIC STENOSIS, MEMBRANOUS</a>	OMIM		MGI
<a href="#">MILLER-DIEKER SYNDROME (MDS)</a>	DECIPHER		
<a href="#">CARDIAC ARRHYTHMIA, ANKYRIN-B-RELATED</a>	OMIM	human	IMPC MGI



# CONNECT- Cross-species phenotype comparisons by semantic similarity



# CONNECT- Disease

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

## Potential Disease Models







Disease Name	Source	Disease Gene Ortholog	Syntenic Disease Locus	Mouse Literature Evidence (MGI)	MGI Mouse Phenotype Evidence (Phenodigm)	IMPC Mouse Phenotype Evidence (Phenodigm)	
<a href="#">Gray Platelet Syndrome</a>	<a href="#">OMIM:139090</a>	Yes	Yes	Yes	<b>90.31</b>	<b>62.24</b>	
<a href="#">Gray Platelet Syndrome</a>	<a href="#">ORPHANET:721</a>	Yes			<b>74.61</b>	<b>55.79</b>	
<a href="#">Platelet Signal Processing Defect</a>	<a href="#">OMIM:173590</a>				<b>91.37</b>	<b>67.05</b>	

# CONNECT-Disease pages

## Disease: Hermansky-Pudlak Syndrome













**Name** Hermansky-Pudlak Syndrome 7  
**Synonyms** -  
**Locus** 6p22.3  
**Associated Human Genes** [DTNBP1](#)  
**Mouse Orthologs** [Dtnbp1](#)  
**Source** [OMIM:614076](#)

**OMIM:614076 Disease Phenotype Terms**




-  Bruising susceptibility
-  Albinism
-  Ocular albinism
-  Impaired platelet aggregation

**Associated Mouse Models (PhenoDigm predicted)**












**78.96: [Dtnbp1<sup>sdv</sup>/Dtnbp1<sup>sdv</sup>](#)** involves: DBA/2J (Source: MGI)

-  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<sup>sdv</sup>/Dtnbp1<sup>sdv</sup>](#)** DBA/2J-Dtnbp1/J (Source: MGI)

-  diluted coat color
-  decreased eye pigmentation
-  increased bleeding time

**66.52: [Dtnbp1<sup>tm1b\(EUCOMM\)Hmgu</sup>/Dtnbp1<sup>tm1b\(EUCOMM\)Hmgu</sup>](#)** C5

-  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
-  increased circulating glucose level
-  decreased mean corpuscular hemoglobin concentration

## Potential Mouse Models

Mouse Gene Symbol	Disease Gene Ortholog	Syntenic Disease Locus	Mouse Literature Evidence (MGI)	MGI Mouse Phenotype Evidence (Phenodigm)	IMPC Mouse Phenotype Evidence (Phenodigm)	
<a href="#">Dtnbp1</a>	Yes	Yes	Yes	<b>78.96</b>	<b>66.52</b>	
<a href="#">Hps3</a>				<b>88.9</b>		
<a href="#">Tyr</a>				<b>87.95</b>		



# CONNECT-Disease gene discovery

## Disease: Malignant Hyperthermia, Susceptibility To, 3

**Name** Malignant Hyperthermia, Susceptibility To, 3  
**Synonyms** MHS3  
**Locus** 7q21-q22  
**Associated Human Genes** -  
**Mouse Orthologs** -  
**Source** [OMIM:154276](#)

**OMIM:154276 Disease 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

**Associated Mouse Models (PhenoDigm predicted)**

**77.67: [Gpc2<sup>tm1.1\(KOMP\)Vlcg</sup>/+](#) C57BL/6NCrl** (Source: [PhenoDigm](#))

- increased circulating phosphate level
- increased circulating chloride level
- decreased circulating chloride level
- increased circulating bilirubin level
- decreased blood urea nitrogen level
- increased circulating sodium level
- decreased circulating sodium level

**57.12: [Gpc2<sup>tm1.1\(KOMP\)Vlcg</sup>/Gpc2<sup>tm1.1\(KOMP\)Vlcg</sup>](#) C57BL/6NCrl**

- decreased neutrophil cell number
- decreased body weight
- decreased basophil cell number
- decreased eosinophil cell number
- decreased circulating potassium level
- decreased mean platelet volume

### Potential Mouse Models

Mouse Gene Symbol	Disease Gene Ortholog	Syntenic Disease Locus	Mouse Literature Evidence (MGI)	MGI Mouse Phenotype Evidence (Phenodigm)	IMPC Mouse Phenotype Evidence (Phenodigm)
<a href="#">Gpr22</a>		Yes			71.39 +
<a href="#">Gpc2</a>		Yes			77.67 +



# CONNECT-Data download

Search      About IMPC      News & Events      Contact My IMPC      [Release: 1.1](#) **[Ftp](#)** [License](#) [Changelog](#)

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Documentation

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## Index of ftp://ftp.ebi.ac.uk/pub/databases/impc/release-1.1/

 [Up to higher level directory](#)

Name	Size	Last Modified
 <a href="#">csv</a>		29/06/2014 14:27:00
 <a href="#">mysql</a>		29/06/2014 13:24:00





# CONNECT- RESTFUL API

<https://github.com/mipi2/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>

```
- <doc>
  <double name="intercept_estimate">5.752570152282715</double>
  <double name="group_2_residuals_normality_test">0.613398015499115</double>
  <double name="genotype_effect_stderr_estimate">0.3152709901332855</double>
  <double name="group_1_residuals_normality_test">0.39963701367378235</double>
  <int name="male_control_count">8</int>
  <bool name="variance_significant">true</bool>
  <str name="zygosity">homozygote</str>
  <str name="data_type">unidimensional</str>
  <int name="female_mutant_count">8</int>
  <str name="status">Success</str>
  <bool name="batch_significant">false</bool>
  <double name="sex_effect_stderr_estimate">0.3152709901332855</double>
  <double name="interaction_effect_p_value">0.12988199293613434</double>
  <str name="dependent_variable">ESLIM_009_001_703</str>
  <int name="control_biological_model_id">2</int>
  <str name="doc_id">ESLIM_009_001_703_1</str>
  <double name="sex_effect_p_value">0.07062750309705734</double>
  <double name="intercept_estimate_stderr_estimate">0.26645299792289734</double>
  <double name="p_value">0.04863490164279938</double>
  <int name="male_mutant_count">6</int>
  <str name="colony_id">HEPD0528_4_A08</str>
  <double name="genotype_effect_parameter_estimate">-0.6093779802322388</double>
  <double name="null_test_p_value">0.04863490164279938</double>
  <int name="db_id">1</int>
  <str name="metadata_group">b114ce3ef8bb816cc6b14ec12f0314c8</str>
  <str name="group_2_genotype">HEPD0528_4_A08</str>
```

# Lets Explore

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