

Human-Mouse: Disease Connection Module

You have an exome sequencing result come back for a patient who as a familial susceptibility to glomerulonephritis (*renal/urinary system phenotype*), vasculitis (*cardiovascular system phenotype*), and leukemia (*tumorigenesis phenotype*), which appears to be inherited as a monogenic trait. The genes with predicted pathogenic variants are: *ACOX1*, *CHAT*, *SH2D3C*, *TUSC2* and *ZYX*.

For the following problems, use the **Human-Mouse: Disease Connection**, which has a link from MGI's homepage, or can be accessed directly at: <http://diseasemodel.org>

15. Based on mouse phenotypic annotations, which of these genes is the most likely candidate for your observations?
- ACOX1*
 - CHAT*
 - SH2D3C*
 - TUSC2*
 - ZYX*

Enter the list of 5 genes into the “Search by genes” box on the HMDC home page and press “GO”.

On the **Gene Homologs x Phenotypes/Diseases** grid that appears, locate the “renal/urinary system”, “cardiovascular system”, and “tumorigenesis” columns in the **Mammalian Phenotype** portion of the grid. You can place a check mark in boxes above each column in order to highlight (as shown), or, for a larger list, you may want to apply these as filters. This will restrict the table to retain only those columns/rows which have data in within the selected.

Blue shading in the cells indicate that at least one mouse mutant genotype has a phenotypic annotation within the system, and from this list, *Tusc2* is the only gene annotated to all three systems. Clicking on the individual cells at the intersection of *Tusc2*-cardiovascular system, *Tusc2*-renal/urinary system or *Tusc2*-tumorigenesis opens a pop-up window where the alleles and more specific phenotypes are displayed. Glomerulonephritis, vasculitis and leukemia all appear in these pop-ups.

You can drill down further to locate a mutation description for the allele, it's complete phenotypic profile (as reported), associated references, and to locate mice by clicking on the hyperlinked **Allele Symbol** to go to the corresponding MGI **Allele Detail page**.

Results

You searched for: Genes matching [CHAT, ACOX1, SH2D3C, TUSC2 ZYX]

Gene Homologs x Phenotypes/Diseases | Genes (19) | Diseases (2)

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

Human Gene	Mouse Gene	behavior/neurological	cardiovascular system	cellular	endocrine/exocrine glands	growth/size	hematopoietic system	homeostatic/metabolism	immune system	liver/biliary system	mortality/aging	muscle	nervous system	renal/urinary system	reproductive system	tumor/leukemia	normal phenotype	Adrenoleukodystrophy	Wagtail-like
ACOX1	Acox1																		
CHAT	Chat																		
SH2D3C	Sh2d3c																		
TUSC2	Tusc2																		
ZYX	Zyx																		

Data for Tusc2 and cardiovascular system abr

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

Mouse Genotype	glomerular capillary thrombo-	vasculitis	arteritis
Tusc2^{tm1Avi}/Tusc2^{tm1Avi}			
Tusc2^{tm1Avi}/Tusc2⁺			

16. Which of these genes would be expected to be associated with infertility (a *reproductive system* phenotype)?

- a) *Acox1*
 b) *Chat*
 c) *Sh2d3c*
 d) *Tusc2*
 e) *Zyx*

Remove any filters that were applied in the previous question. Examining the Gene Homologs x Phenotypes/Diseases grid for reproductive system, shows that three of the genes (*Acox1*, *Chat*, *Sh2d3c*) have some annotated data from mouse mutants.

Clicking on the intersection of *Acox1*-*reproductive system* generates a pop-up with both male and female infertility annotations reported, making this a good candidate gene for an infertility effect.

The *Chat*-*reproductive system* intersection is marked by an “N” which indicates that some aspects of the reproductive system have been examined in mutants and reported as “normal”, with no abnormal phenotypes reported within the system.

The *Sh2d3c*-*reproductive system* pop-up shows an annotation to “small testis” which can be associated with reduced fertility, but is not as promising a candidate as the *Acox1*.

Gene Homologs x Phenotypes/Diseases Genes (19) Diseases (2)

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...](#)

Apply Filters: Retain selected col/rows

Human Gene	Mouse Gene	behavior/neurological	cardiovascular system	cellular	endocrine/exocrine glands	growth/size	hematopoietic system	homeostasis/metabolism	immune system	liver/biliary system	mortality/aging	muscle	nervous system	renal/urinary system	reproductive system
ACOX1	Acox1														N
CHAT	Chat														
SH2D3C	Sh2d3c														
TUSC2	Tusc2														
ZYX	Zyx														

Data for Acox1 and reproductive system

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

Mouse Genotype	small ovary	Leydig cell hypoplasia	small testis	abnormal spermatogenesis	abnormal spermatid morphology	female infertility	male infertility	reduced fertility
Acox1 ^{lampe1} /Acox1 ^{lampe1}								
Acox1 ^{tm1Jkr} /Acox1 ^{tm1Jkr}								

17. Which of these genes has variants associated with **Myasthenic Syndrome, Congenital, Associated with Episodic Apnea** in human patients?

- a) *ACOX1*
 b) *CHAT*
 c) *SH2D3C*
 d) *TUSC2*
 e) *ZYX*

The *CHAT* gene has an orange fill at the intersection of *CHAT*-*Myasthenic Syndrome* indicating a human gene-disease annotation from OMIM.

You can also use the **Diseases** tab to locate this information. On this tab, click the hyperlinked disease name to go to the **Human Disease and Mouse Model detail** page in MGI.

Gene Homologs x Phenotypes/Diseases Genes (19) Diseases (2)

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...](#)

Apply Filters: Retain selected col/rows


Human Gene	Mouse Gene	behavior/neurological	cardiovascular system	cellular	endocrine/exocrine glands	growth/size	hematopoietic system	homeostasis/metabolism	immune system	liver/biliary system	mortality/aging	muscle	nervous system	renal/urinary system	reproductive system
ACOX1	Acox1														
CHAT	Chat														
SH2D3C	Sh2d3c														
TUSC2	Tusc2														
ZYX	Zyx														

Gene Homologs x Phenotypes/Diseases Genes (19) Diseases (2)

Export: [Text File](#)

Disease	OMIM ID	Mouse Models	Associated Mouse Genes	Associated Human Genes	References using Mouse Models
Myasthenic Syndrome, Congenital, Associated with Episodic Apnea	254210			CHAT	
Peroxisomal Acyl-CoA Oxidase Deficiency	264470	1	Acox1	ACOX1	1





References associated with this Gene


Symbol	Acox1
Name	acyl-Coenzyme A oxidase 1, palmitoyl
ID	MGI:1330812

Displaying only references relevant to disease models.

1 reference(s) Filters: No filters selected. Filter these references below.

Export:

Filter references by:

PubMed ID MGI Ref. ID	Author(s)	Title	Curated Data
8798738  1:35794	Fan CY; Pan J; Chu R; Lee D; Kluckman KD; Usuda N; Singh I; Yeldandi AV; Rao MS; Maeda N; Reddy JK	Hepatocellular and hepatic peroxisomal alterations in mice with a disrupted peroxisomal fatty acyl-coenzyme A oxidase gene.	<ul style="list-style-type: none"> Functional annotations Genome features: 1 Phenotypic alleles: 1

abstract ▾

Peroxisomal genetic disorders, such as Zellweger syndrome, are characterized by defects in one or more enzymes involved in the peroxisomal