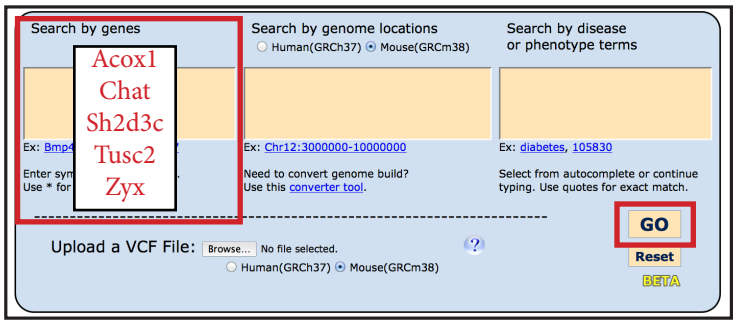
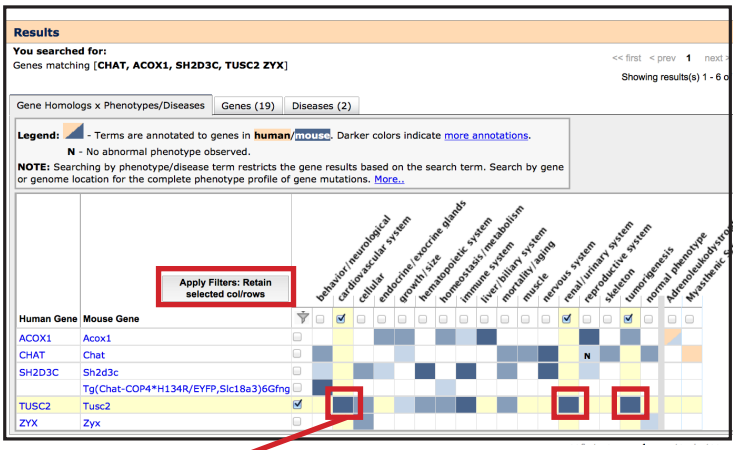
Human-Mouse: Disease Connection Module

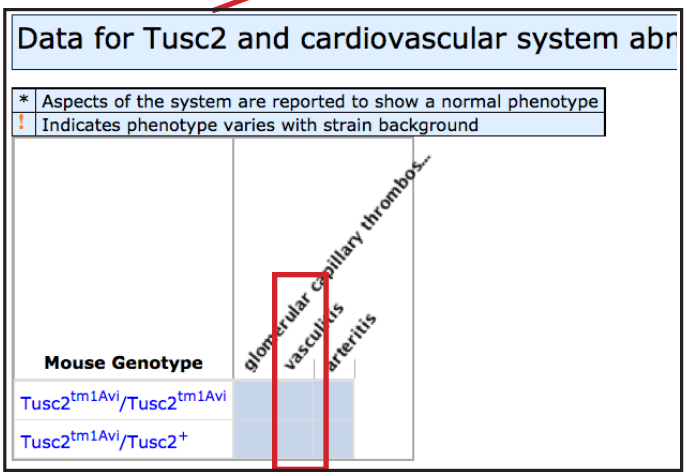
You have an exome sequencing result come back for a patient who as a familial susceptibility to glomerulonephritis (*renal/urinary system phenotype*), vasculitis (*cardiovascular system phenotype*), and leukemia (*tumorigenesis phenotype*), which appears to be inherited as a monogenic trait. The genes 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?
    a) *ACOX1*
    b) *CHAT*
    c) *SH2D3C*
    d) *TUSC2*
    e) *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 windown 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**.

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

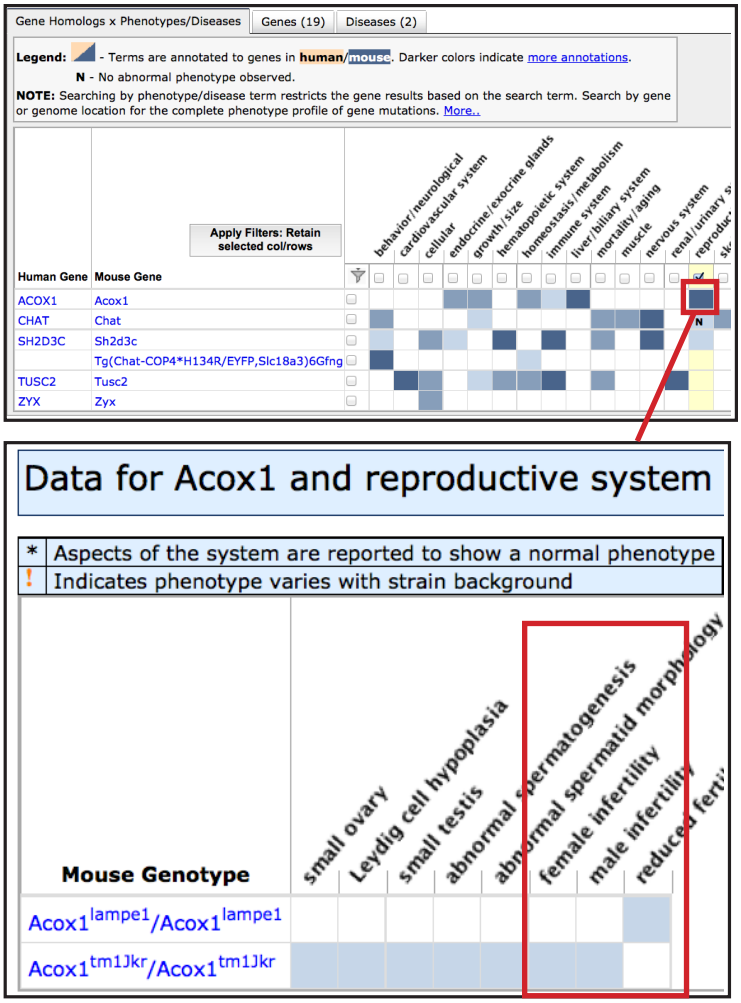
a) *Acox1*
b) *Chat*
c) *Sh2d3c*
d) *Tusc2*
e) *Zyx*

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

Clicking on the intersectionof *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*.

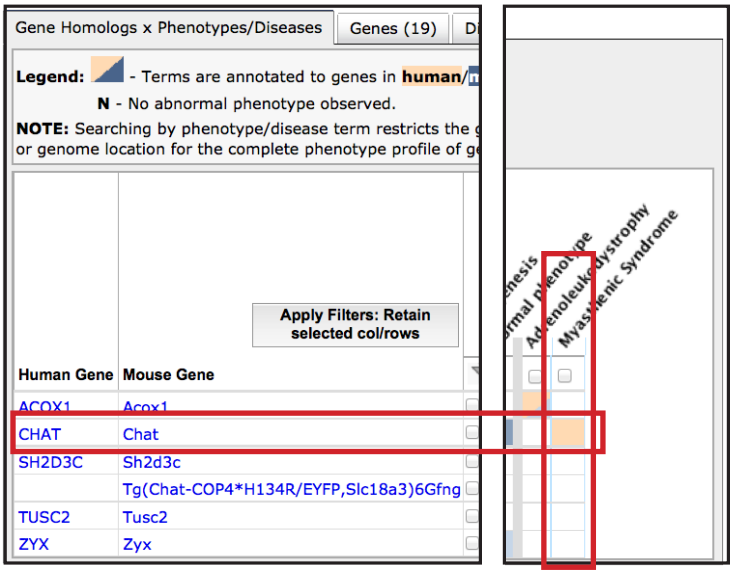


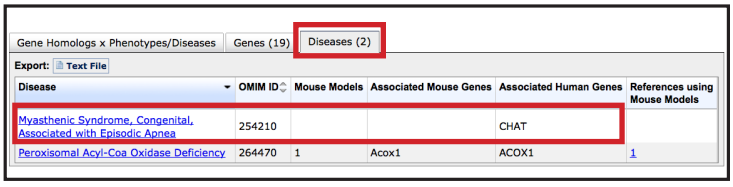
17. Which of these genes has variants associated with **Myasthenic Syndrome, Congenital, Associated with Episodic Apnea** in human patients?

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

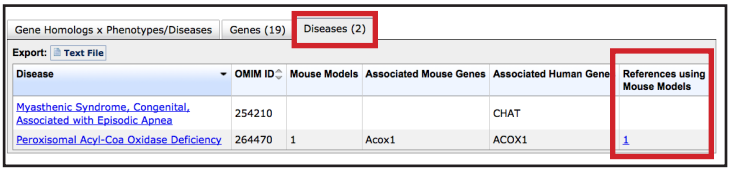
The *CHAT* gene has an orange fill at the intersection of *CHAT-Myasthemic Syndrome* indicating a human gene-disease annotation from OMIM.

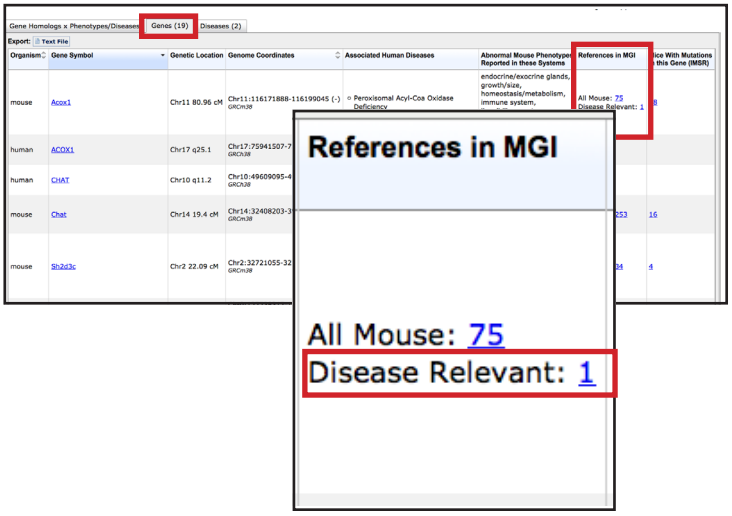
You can also use the **Diseases** tab to locate this information. On this tab, click the hyperlinked disease name to go the a **Human Disease and Mouse Model detail page** in MGI.

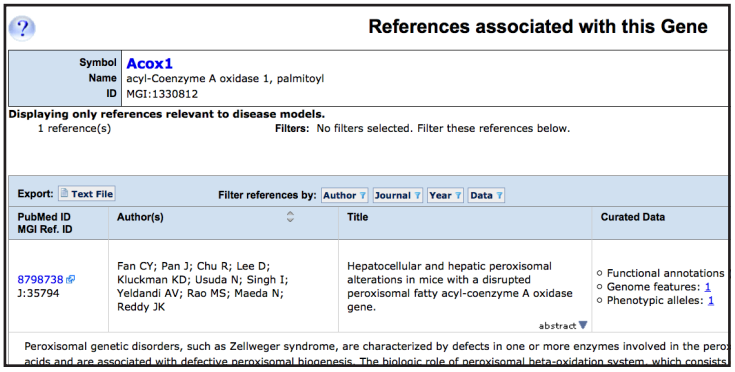




18. What is the **Disease Relevant** publication that describes the association of mouse *Acox1* in **Peroxisomal Acyl-Coa Oxidase Deficiency**?
    a) Abbott BD et al. (2012) Reprod. Toxicol.
    b) Huang J et al. (2011) Am. J. Pathol.
    c) Fan CY et al. (1996) J. Biol. Chem.
    d) Suzuki et al. (1994) J. Pediat.
    e) This association was made by Mouse Genome Informatics curators.







This information can be accessed off of the **Diseases** or **Genes** tabs.

On the **Diseases** tab, only disease-relevant mouse publications are reported, in the column titled: "**References using Mouse Models**".

On the **Genes** tab, all mouse references in MGI for the gene are linked in the **References in MGI** column, with a subset pulled out for "**Disease Relevant:"**.

Click on the hyperlinked number to see the citation and link to the original article, in this case, the Fan et al. (1996) paper.

MGI curators never make gene-disease associations without a peer-reviewed author statement as a reference.

For any questions, please contact:

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