

Ctsh Cas9-CKO Strategy

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Project Overview

Project Name

Ctsh

Project type

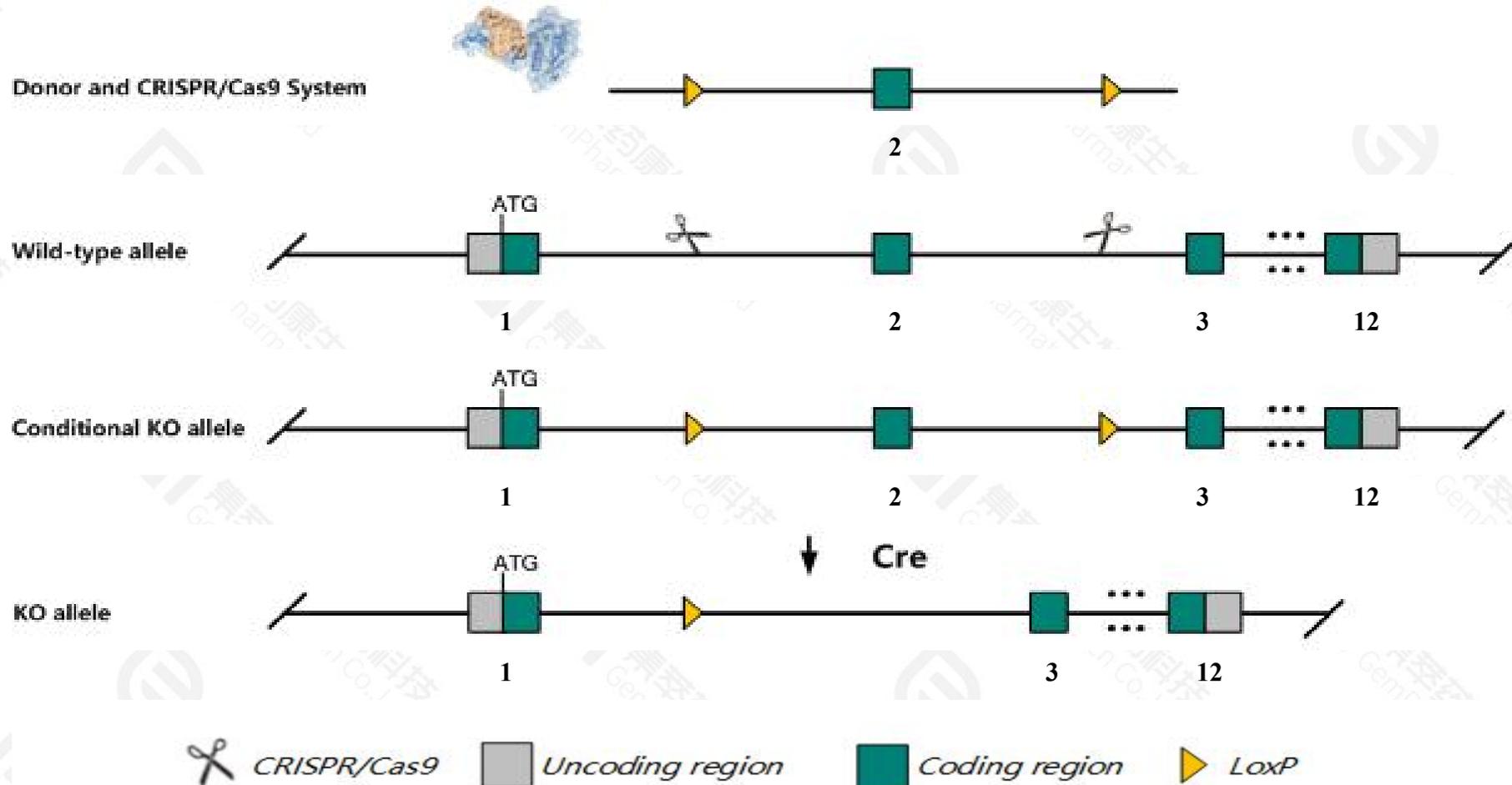
Cas9-CKO

Strain background

C57BL/6JGpt

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Ctsh* gene. The schematic diagram is as follows:



- The *Ctsh* gene has 11 transcripts. According to the structure of *Ctsh* gene, exon2 of *Ctsh-201*(ENSMUST00000034915.15) transcript is recommended as the knockout region. The region contains 32bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Ctsh* gene. The brief process is as follows: CRISPR/Cas9 system and Donor were microinjected into the fertilized eggs of C57BL/6JGpt mice. Fertilized eggs were transplanted to obtain positive F0 mice which were confirmed by PCR and sequencing. A stable F1 generation mouse model was obtained by mating positive F0 generation mice with C57BL/6JGpt mice.
- The flox mice will be knocked out after mating with mice expressing Cre recombinase, resulting in the loss of function of the target gene in specific tissues and cell types.

- According to the existing MGI data, mice homozygous for a reporter allele exhibit impaired lung surfactant and an abnormal eye globe with elongated axial length.
- The *Ctsh* gene is located on the Chr9. If the knockout mice are crossed with other mice strains to obtain double gene positive homozygous mouse offspring, please avoid the two genes on the same chromosome.
- This strategy is designed based on genetic information in existing databases. Due to the complexity of biological processes, all risk of loxp insertion on gene transcription, RNA splicing and protein translation cannot be predicted at existing technological level.

Gene information (NCBI)

Ctsh cathepsin H [Mus musculus (house mouse)]

Gene ID: 13036, updated on 13-Mar-2020

Summary

Official Symbol Ctsh provided by [MGI](#)

Official Full Name cathepsin H provided by [MGI](#)

Primary source [MGI:MGI:107285](#)

See related [Ensembl:ENSMUSG00000032359](#)

Gene type protein coding

RefSeq status REVIEWED

Organism [Mus musculus](#)

Lineage Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus

Also known as AL022844

Summary This gene encodes a member of the peptidase C1 (papain) family of cysteine proteases. Alternative splicing results in multiple transcript variants, at least one of which encodes a preproprotein that is proteolytically processed to generate multiple protein products. These products include the cathepsin H mini, heavy, and light chains. In rat and human, these three chains can associate to form the mature enzyme, which has both aminopeptidase and endopeptidase activities. Homozygous knockout mice for this gene exhibit impaired lung surfactant processing and reduced tumorigenesis in a pancreatic cancer model. Multiple pseudogenes of this gene have been identified in the genome. [provided by RefSeq, Aug 2015]

Expression Broad expression in placenta adult (RPKM 82.3), bladder adult (RPKM 57.4) and 21 other tissues [See more](#)

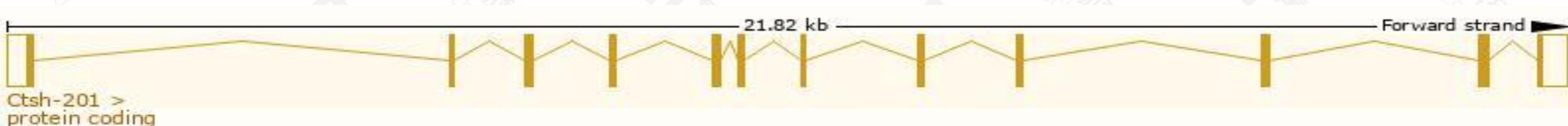
Orthologs [human](#) [all](#)

Transcript information (Ensembl)

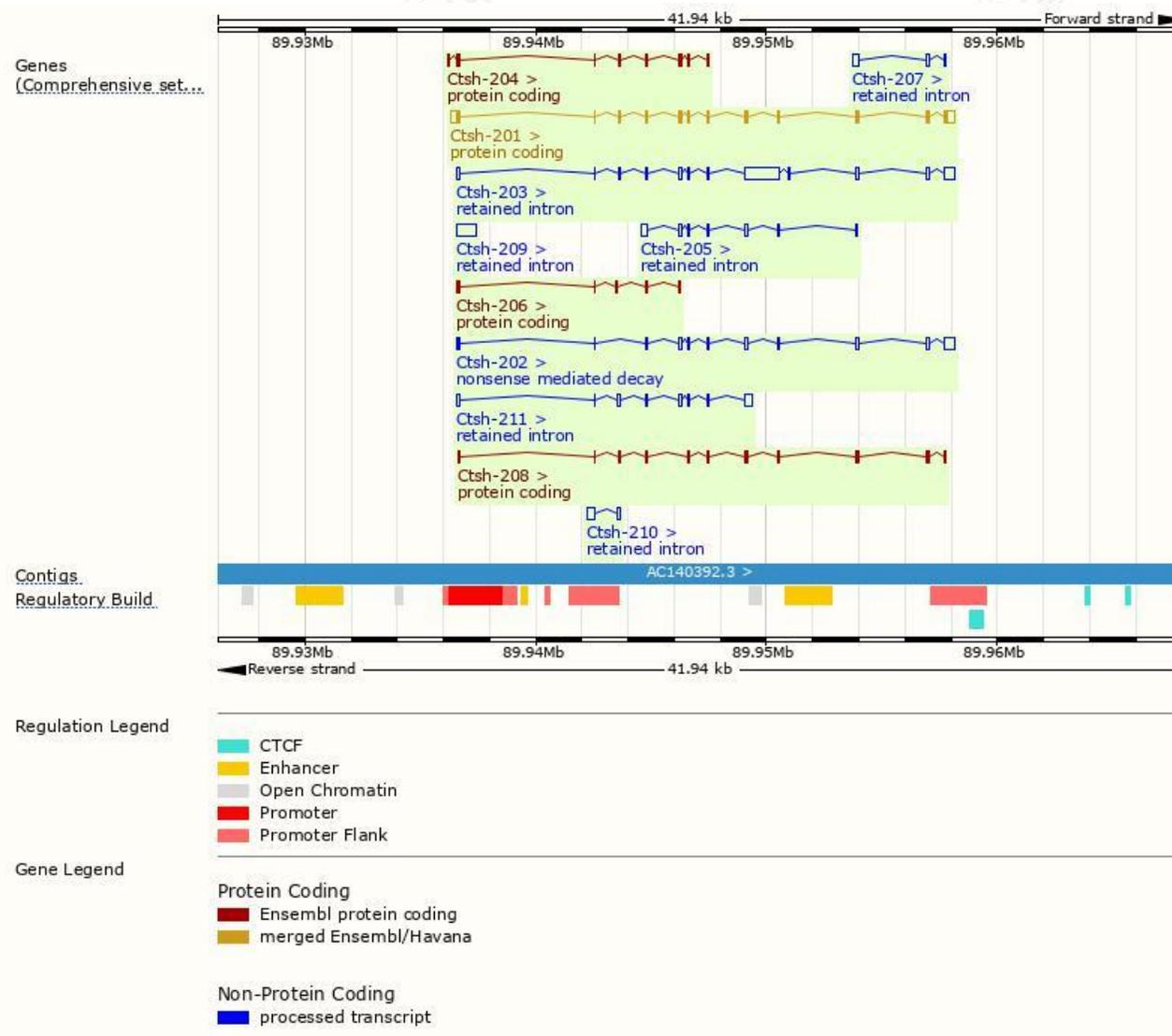
The gene has 11 transcripts, all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Ctsh-201	ENSMUST0000034915.14	1617	333aa	Protein coding	CCDS23399	P49935	TSL:1 GENCODE basic APPRIS is a system to annotate alternatively spliced transcripts based on a range of computational methods to identify the most functionally important transcript(s) of a gene. APPRIS P2
Ctsh-208	ENSMUST00000185459.1	872	290aa	Protein coding	-	A0A087WR20	5' and 3' truncations in transcript evidence prevent annotation of the start and the end of the CDS. CDS 5' and 3' incomplete TSL:5 APPRIS is a system to annotate alternatively spliced transcripts based on a range of computational methods to identify the most functionally important transcript(s) of a gene. APPRIS ALT2
Ctsh-204	ENSMUST00000132718.7	631	198aa	Protein coding	-	D3Z437	CDS 3' incomplete TSL:3
Ctsh-206	ENSMUST00000143172.7	370	119aa	Protein coding	-	D3YVI3	CDS 3' incomplete TSL:3
Ctsh-202	ENSMUST00000123320.7	1238	41aa	Nonsense mediated decay	-	D7UJQ9	TSL:1
Ctsh-203	ENSMUST00000127842.7	2743	No protein	Retained intron	-	-	TSL:2
Ctsh-211	ENSMUST00000190338.6	873	No protein	Retained intron	-	-	TSL:3
Ctsh-209	ENSMUST00000186126.1	818	No protein	Retained intron	-	-	TSL:NA
Ctsh-205	ENSMUST00000142750.1	732	No protein	Retained intron	-	-	TSL:3
Ctsh-210	ENSMUST00000187437.1	480	No protein	Retained intron	-	-	TSL:3
Ctsh-207	ENSMUST00000151219.1	424	No protein	Retained intron	-	-	TSL:2

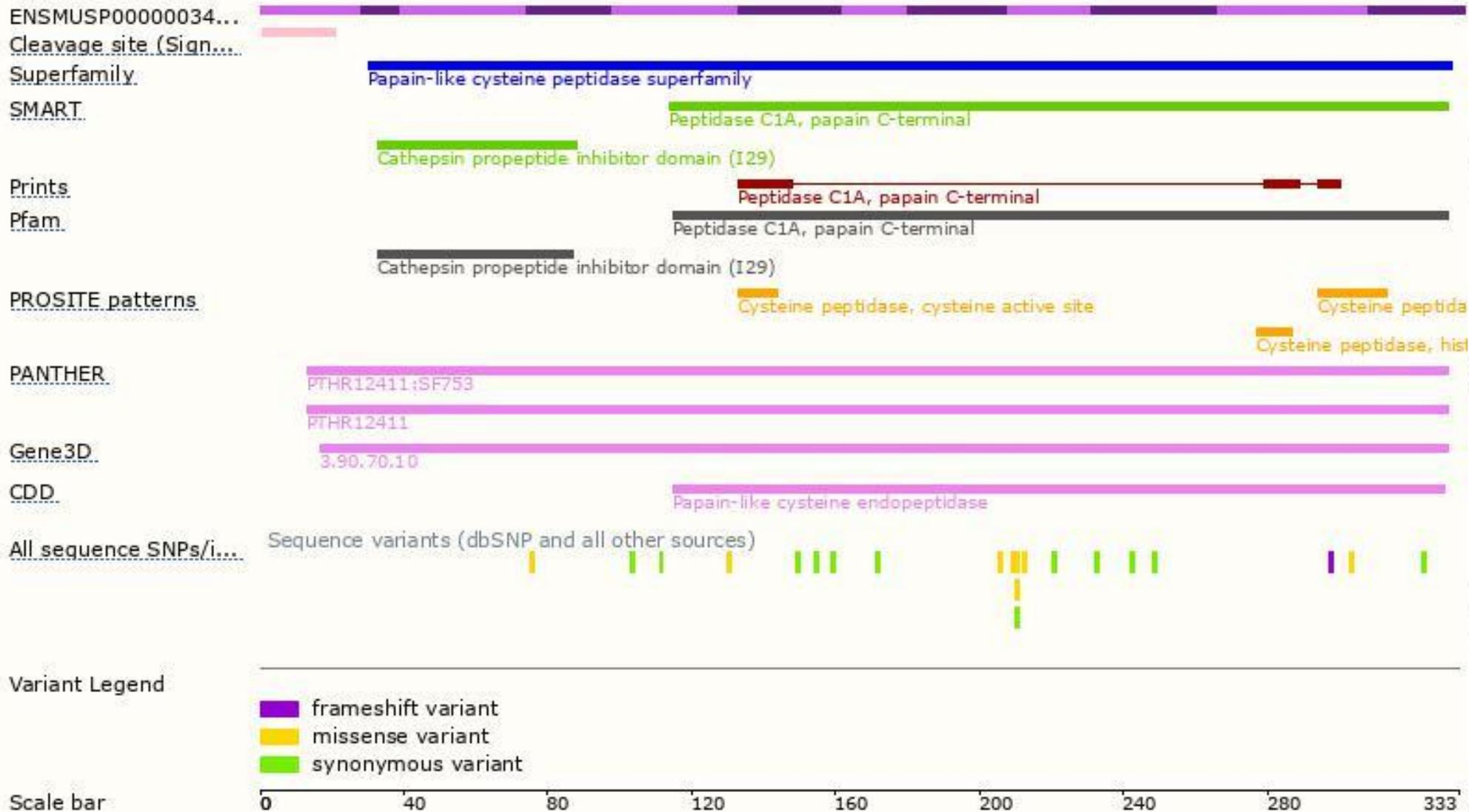
The strategy is based on the design of *Ctsh-201* transcript, the transcription is shown below:



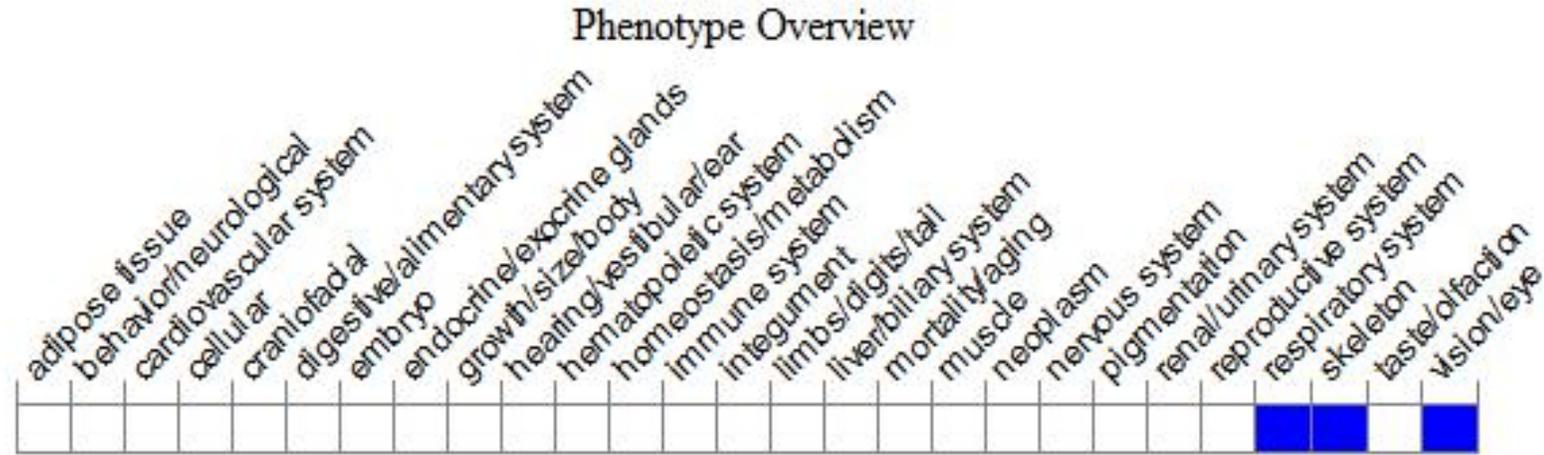
Genomic location distribution



Protein domain



Mouse phenotype description(MGI)



Phenotypes affected by the gene are marked in blue. Data quoted from MGI database(<http://www.informatics.jax.org/>).

According to the existing MGI data, mice homozygous for a reporter allele exhibit impaired lung surfactant and an abnormal eye globe with elongated axial length.

If you have any questions, you are welcome to inquire.

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