

Gcdh Cas9-CKO Strategy

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Reviewer:

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Project Overview

Project Name

Gcdh

Project type

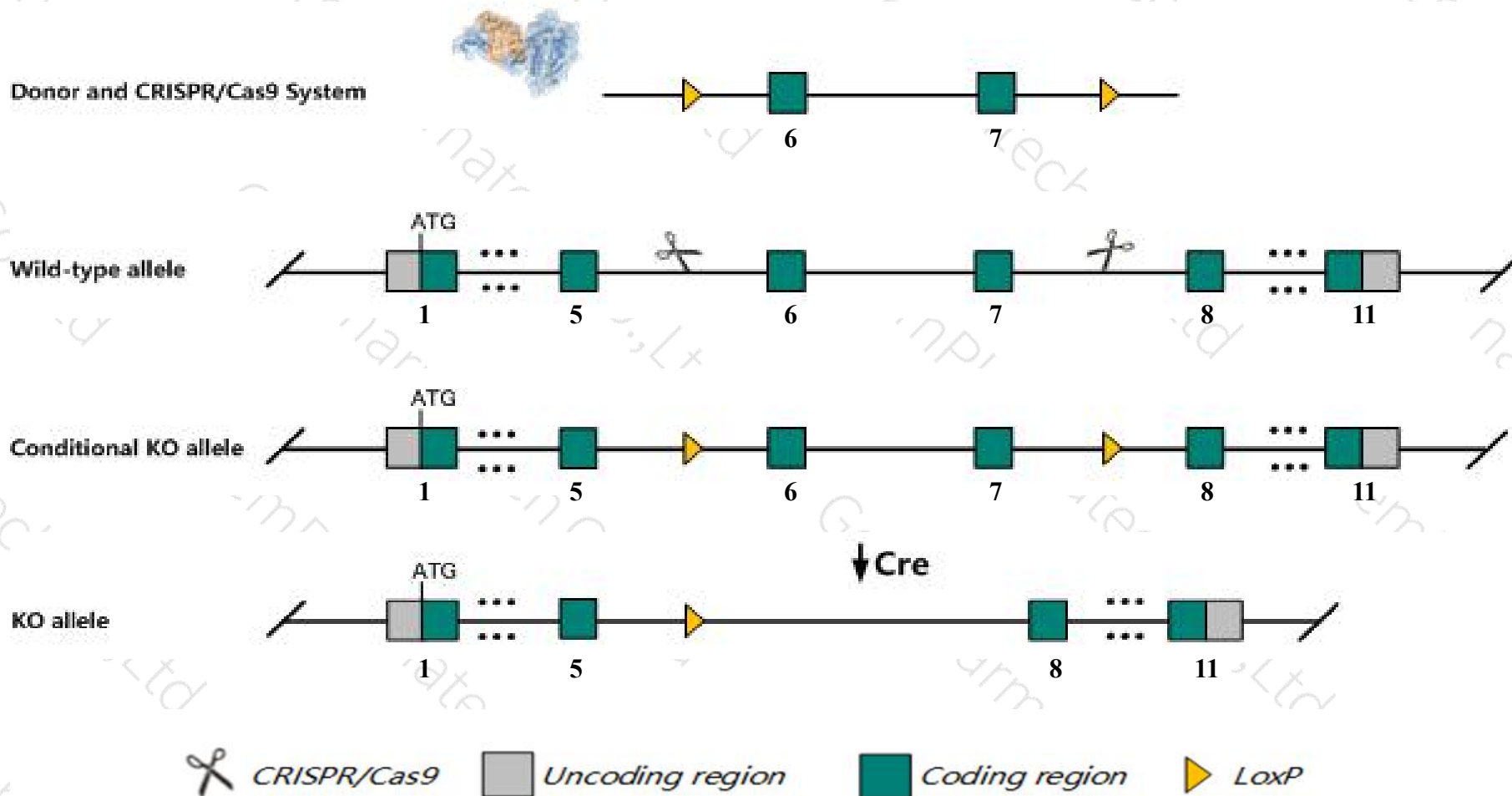
Cas9-CKO

Strain background

C57BL/6JGpt

Conditional Knockout strategy

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



- The *Gcdh* gene has 6 transcripts. According to the structure of *Gcdh* gene, exon6-exon7 of *Gcdh-201* (ENSMUST00000003907.13) transcript is recommended as the knockout region. The region contains 347bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Gcdh* 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, Homozygotes for a targeted null mutation exhibit a mild motor deficit associated with a diffuse spongiform myelinopathy and elevated levels of glutaric acid and 3-hydroxyglutaric acid.
- The N-terminal of *Gcdh* gene will remain several amino acids, it may remain the partial function of *Gcdh* gene.
- Transcript *Gcdh*-206 CDS 3' is incomplete, whether it will be affected is unknown.
- The *Gcdh* gene is located on the Chr8. 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.

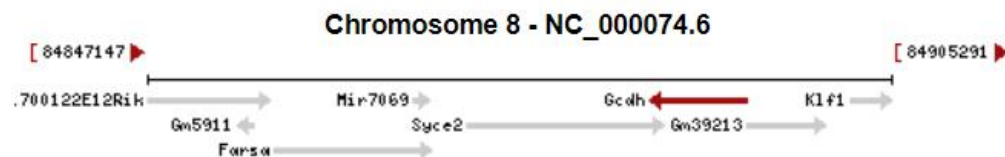
Gene information (NCBI)

Gcdh glutaryl-Coenzyme A dehydrogenase [*Mus musculus* (house mouse)]

Gene ID: 270076, updated on 12-Nov-2019

Summary

Official Symbol	Gcdh provided by MGI
Official Full Name	glutaryl-Coenzyme A dehydrogenase provided by MGI
Primary source	MGI:MGI:104541
See related	Ensembl:ENSMUSG00000003809
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	GCD; D17825; AI266902; 9030411L18
Expression	Biased expression in liver adult (RPKM 212.2), kidney adult (RPKM 105.6) and 13 other tissues See more
Orthologs	human all

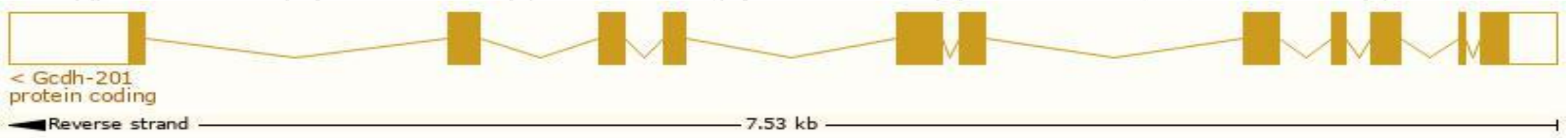


Transcript information (Ensembl)

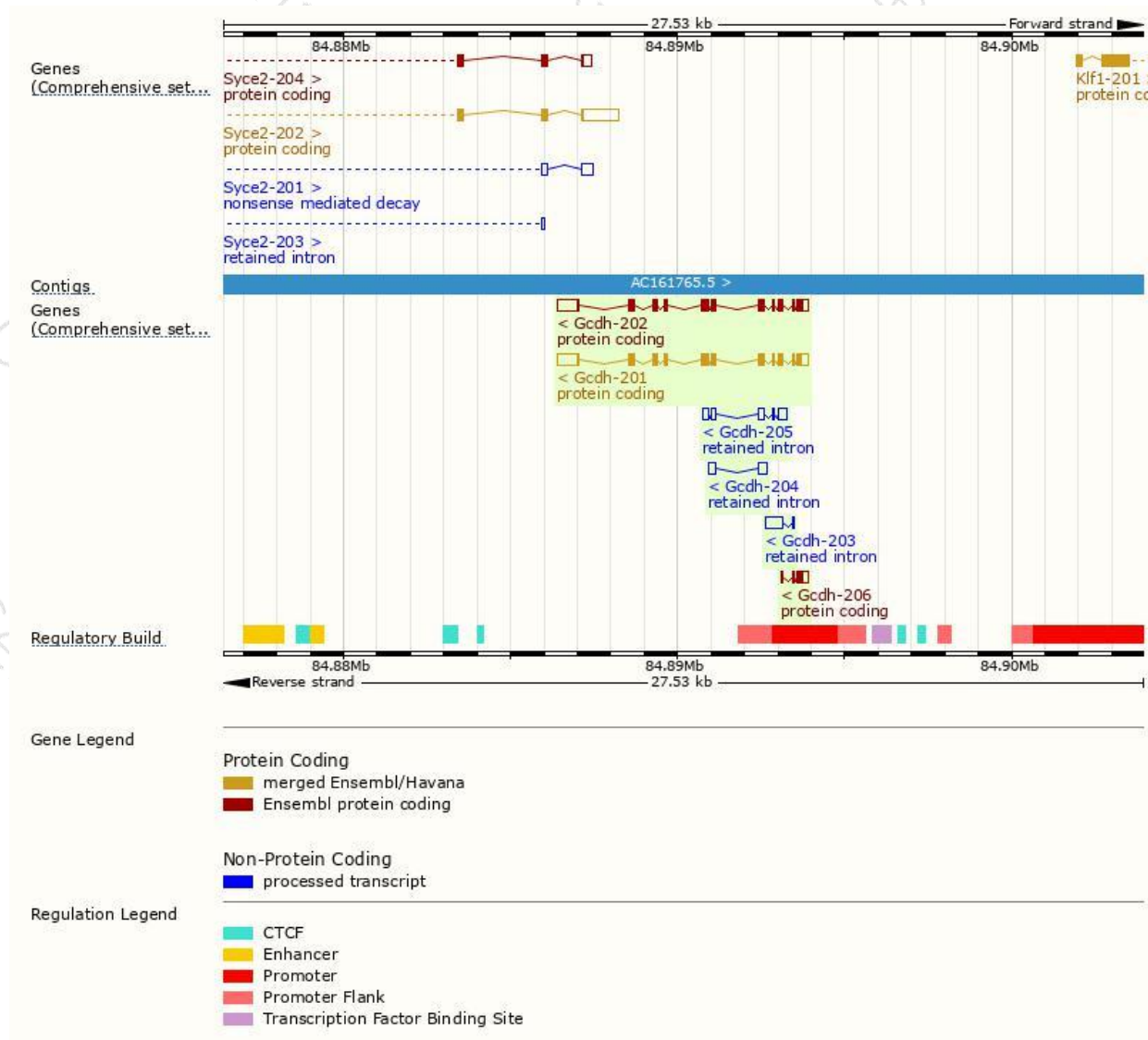
The gene has 6 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Translation ID	Biotype	CCDS	UniProt	Flags
Gcdh-201	ENSMUST00000003907.13	2167	447aa	ENSMUSP00000003907.8	Protein coding	CCDS22482	A0A0A0MQ68	TSL:1 GENCODE basic APPRIS P2
Gcdh-202	ENSMUST00000109745.7	2114	438aa	ENSMUSP00000105367.1	Protein coding	-	Q60759	TSL:5 GENCODE basic APPRIS ALT2
Gcdh-206	ENSMUST00000142748.1	408	75aa	ENSMUSP00000116584.2	Protein coding	-	D3Z4I2	CDS 3' incomplete TSL:2
Gcdh-205	ENSMUST00000139180.1	819	No protein	-	Retained intron	-	-	TSL:2
Gcdh-203	ENSMUST00000128023.1	542	No protein	-	Retained intron	-	-	TSL:5
Gcdh-204	ENSMUST00000136462.1	471	No protein	-	Retained intron	-	-	TSL:3

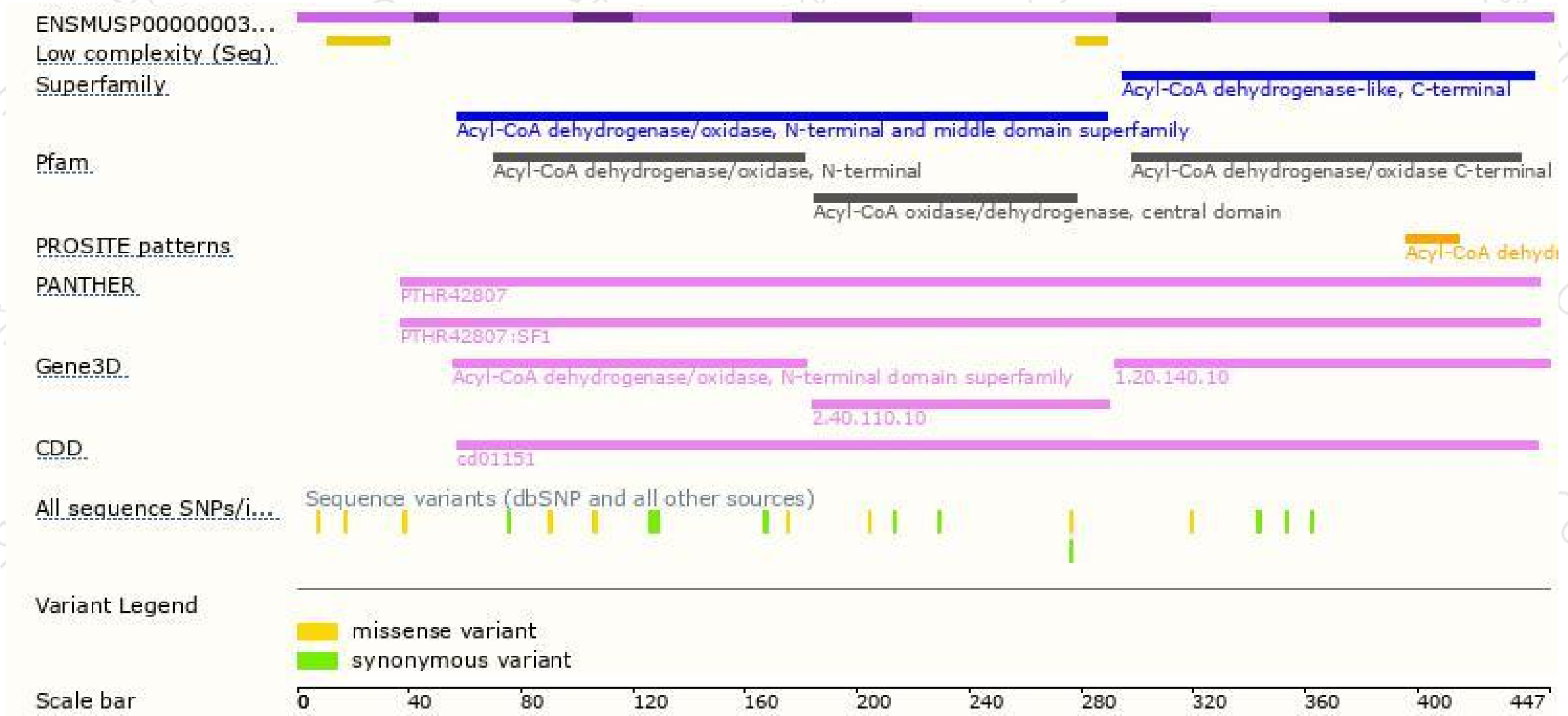
The strategy is based on the design of *Gcdh-201* transcript,The transcription is shown below



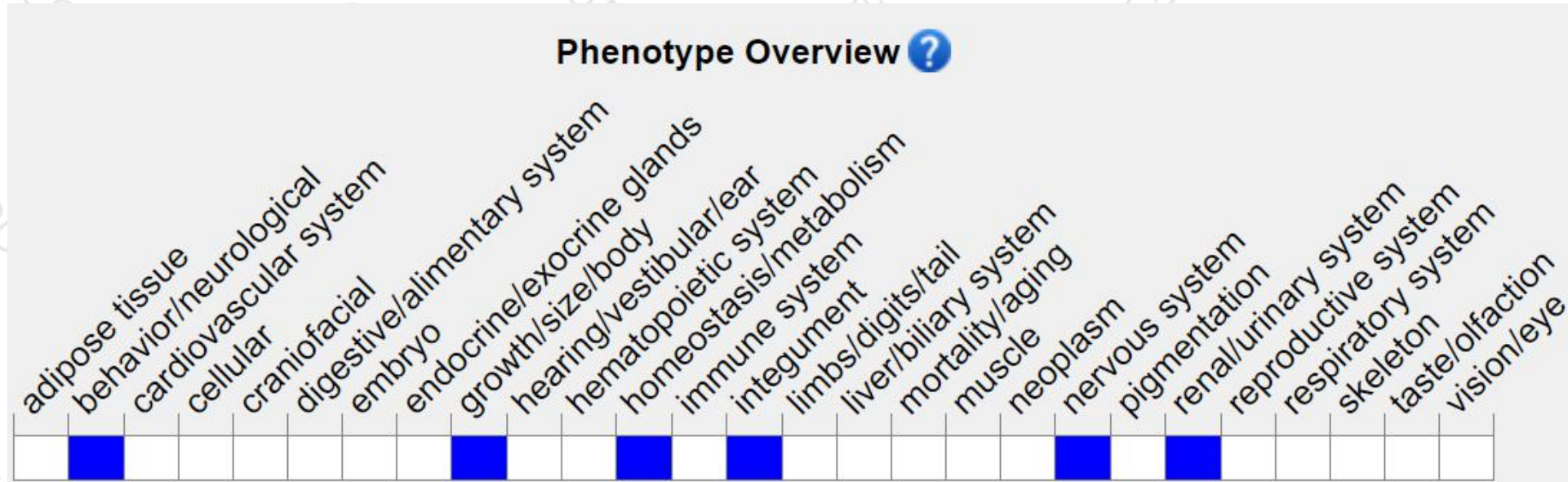
Genomic location distribution



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, Homozygotes for a targeted null mutation exhibit a mild motor deficit associated with a diffuse spongiform myelinopathy and elevated levels of glutaric acid and 3-hydroxyglutaric acid.

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

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