

Cyp46a1 Cas9-CKO Strategy

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Project Overview

Project Name

Cyp46a1

Project type

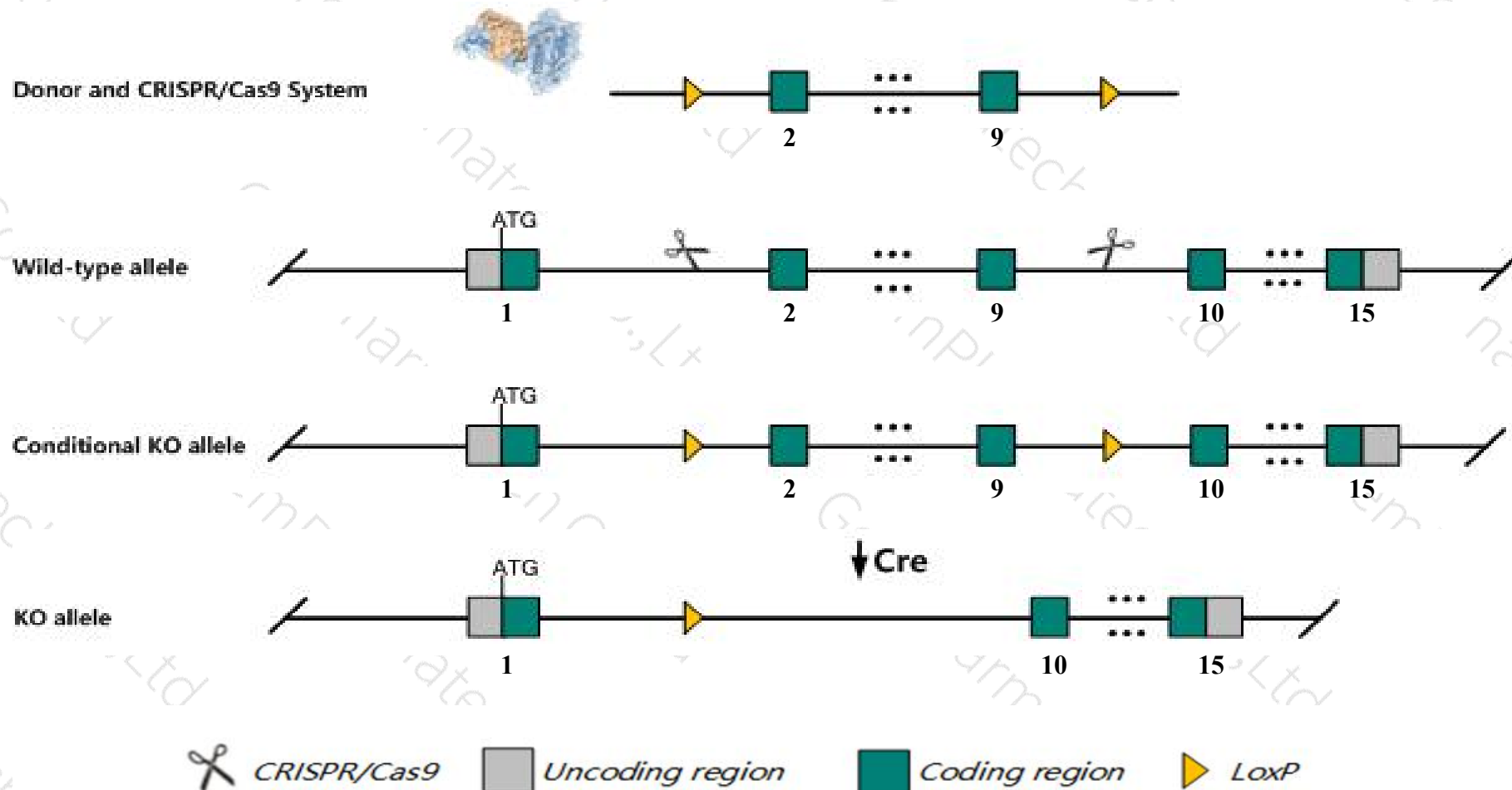
Cas9-CKO

Strain background

C57BL/6JGpt

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Cyp46a1* gene. The schematic diagram is as follows:



- The *Cyp46a1* gene has 4 transcripts. According to the structure of *Cyp46a1* gene, exon2-exon9 of *Cyp46a1-201* (ENSMUST00000021684.5) transcript is recommended as the knockout region. The region contains 788bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Cyp46a1* 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 deletions in this gene are essentially normal. Levels of 24(s)-hydroxycholesterol are reduced in serum and in the brain. Cholesterol synthesis in the brain is reduced 40%.
- The *Cyp46a1* gene is located on the Chr12. 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)

Cyp46a1 cytochrome P450, family 46, subfamily a, polypeptide 1 [*Mus musculus* (house mouse)]

Gene ID: 13116, updated on 26-Oct-2019

Summary

- Official Symbol

Cyp46a1 provided by [MGI](#)
- Official Full Name

cytochrome P450, family 46, subfamily a, polypeptide 1 provided by [MGI](#)
- Primary source

[MGI:MGI:1341877](#)
- See related

[Ensembl:ENSMUSG000000021259](#)
- 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

CH24H; Cyp46
- Expression

Biased expression in cortex adult (RPKM 70.0), frontal lobe adult (RPKM 59.5) and 7 other tissues [See more](#)
- Orthologs

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

Genomic context

Location: 12; 12 F1

See Cyp46a1 in [Genome Data Viewer](#)

Exon count: 16

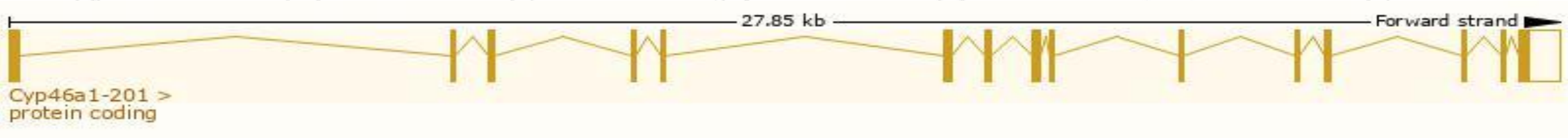
Annotation release	Status	Assembly	Chr	Location
108	current	GRCm38.p6 (GCF_000001635.26)	12	NC_000078.6 (108334268..108362234)
Build 37.2	previous assembly	MGSCv37 (GCF_000001635.18)	12	NC_000078.5 (109572591..109600444)

Transcript information (Ensembl)

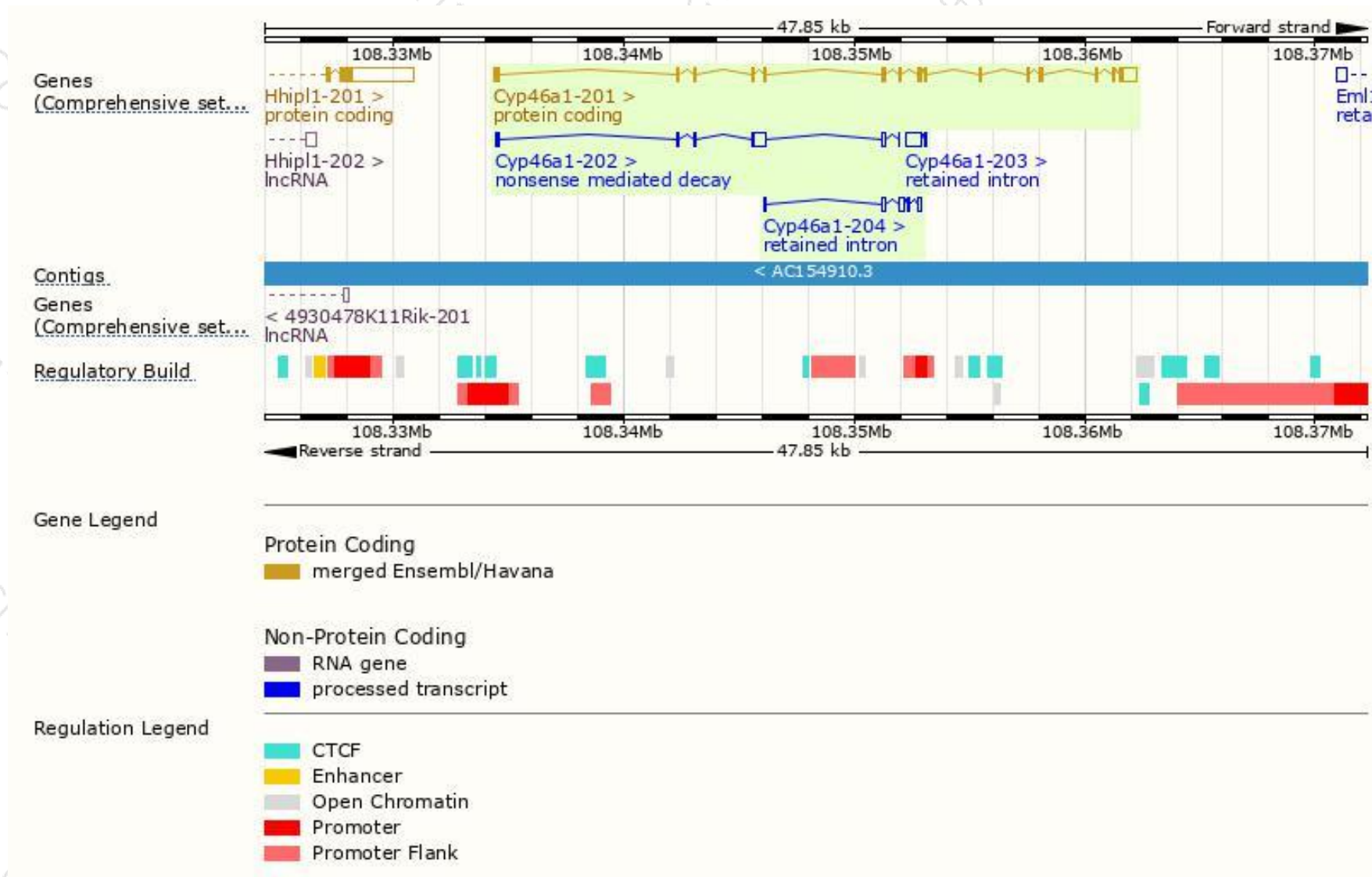
The gene has 4 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Cyp46a1-201	ENSMUST00000021684.5	2118	500aa	Protein coding	CCDS26160	Q3US73 Q9WVK8	TSL:1 GENCODE basic APPRIS P1
Cyp46a1-202	ENSMUST00000221708.1	1034	112aa	Nonsense mediated decay	-	A0A1Y7VM34	CDS 5' incomplete TSL:5
Cyp46a1-203	ENSMUST00000222240.1	764	No protein	Retained intron	-	-	TSL:5
Cyp46a1-204	ENSMUST00000222902.1	733	No protein	Retained intron	-	-	TSL:3

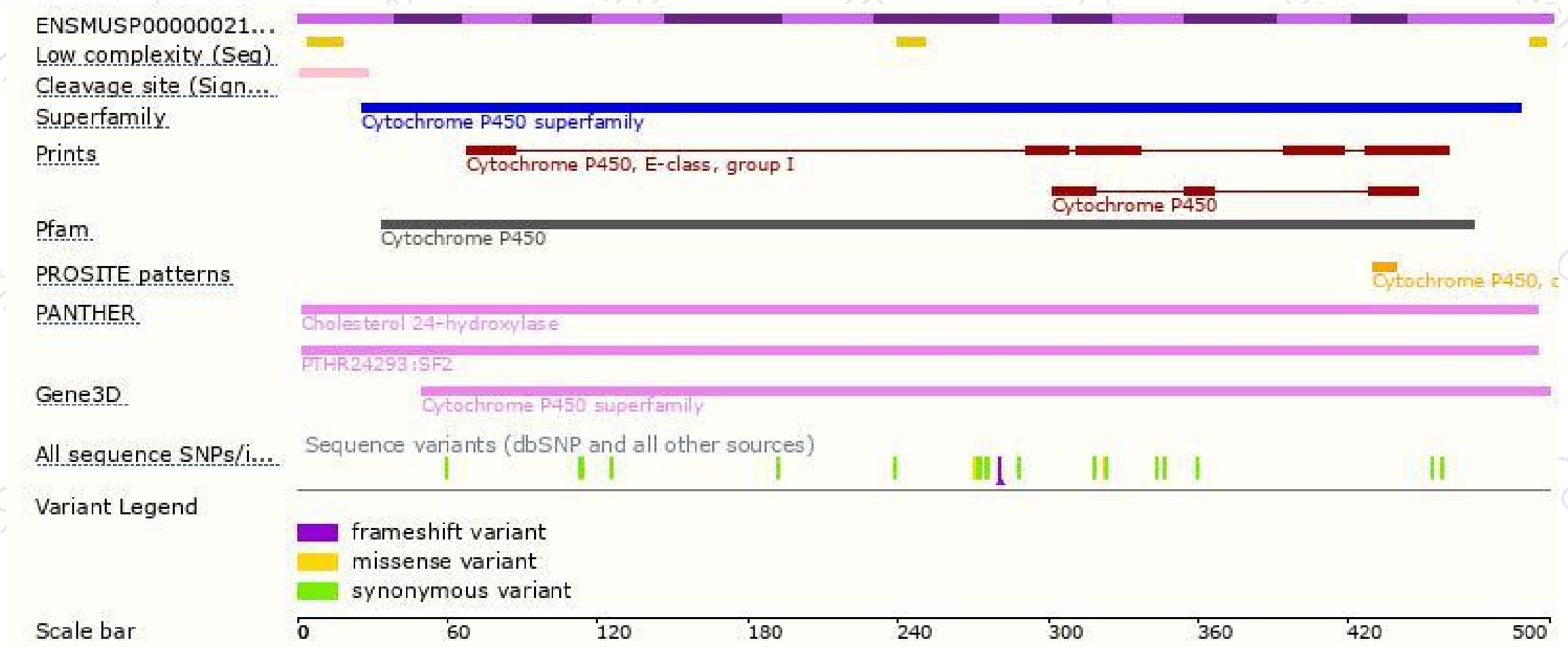
The strategy is based on the design of *Cyp46a1-201* transcript,The transcription is shown below



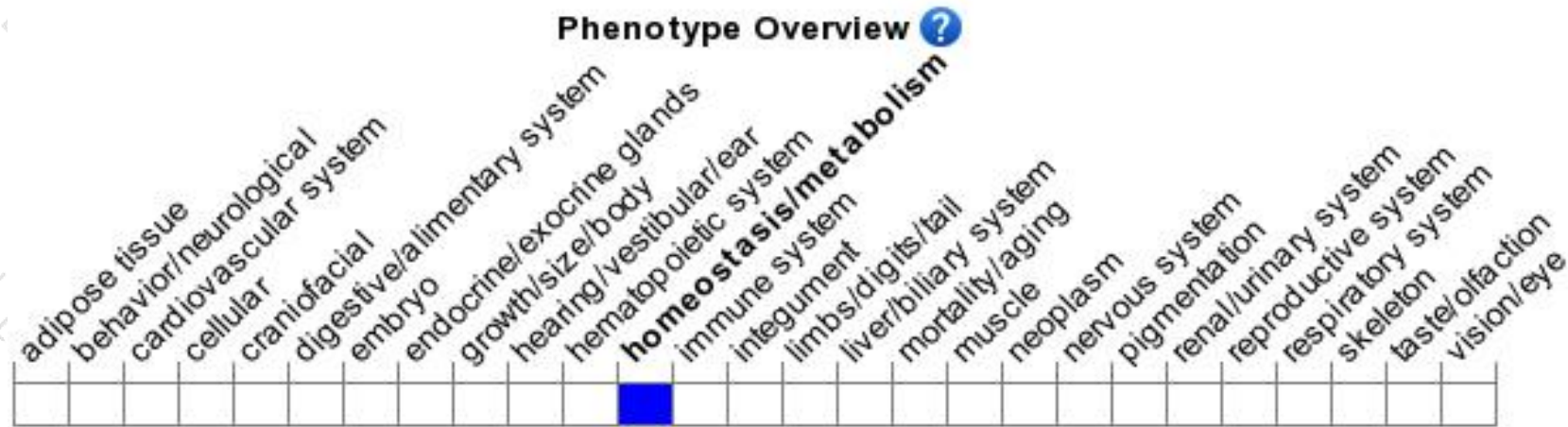
Genomic location distribution



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/>).

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

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