

Lpl Cas9-CKO Strategy

Designer:

Huan Fan

Design Date:

2019-7-25

Project Overview

Project Name

Lpl

Project type

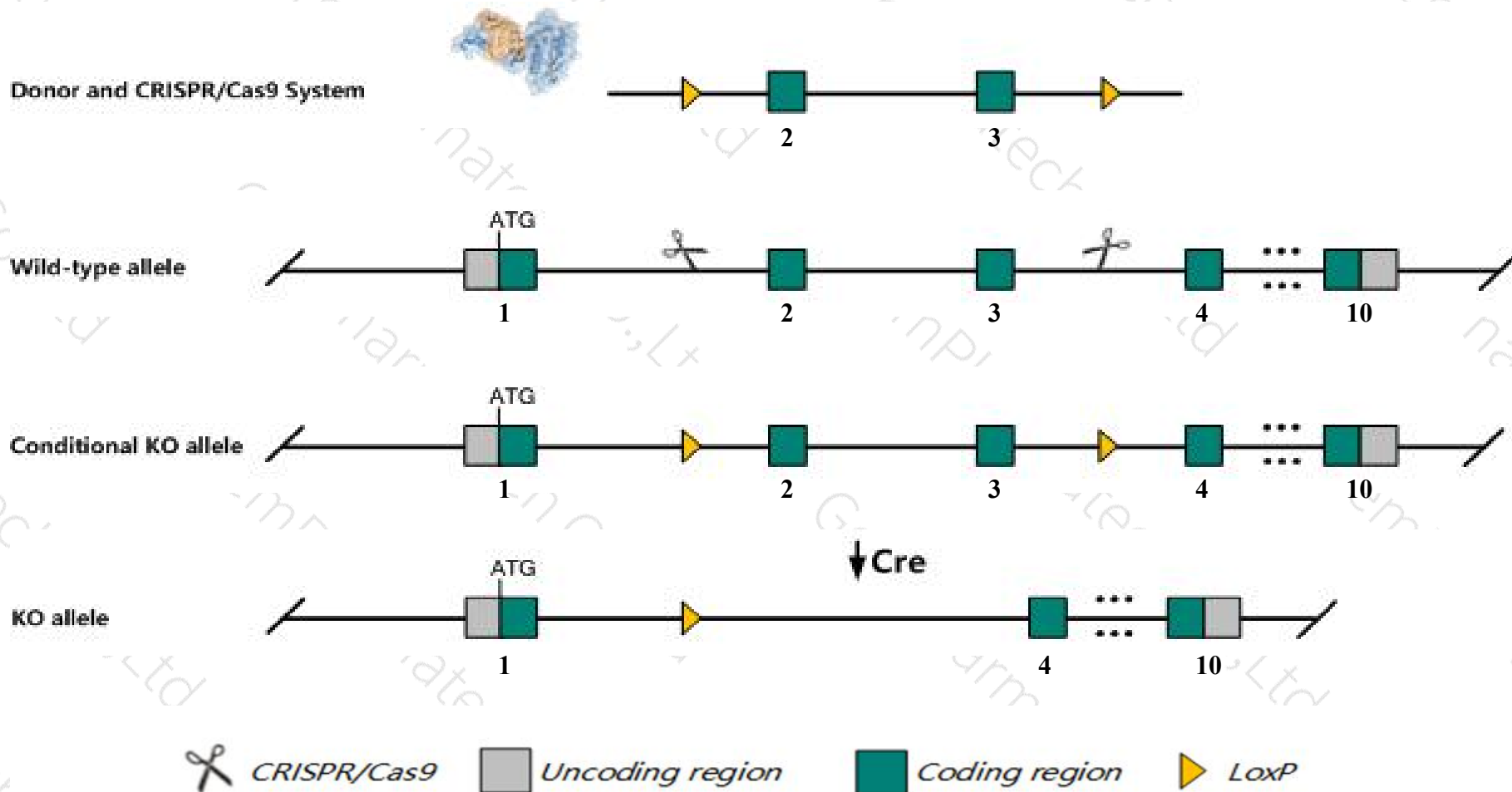
Cas9-CKO

Strain background

C57BL/6JGpt

Conditional Knockout strategy

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



- The *Lpl* gene has 5 transcripts. According to the structure of *Lpl* gene, exon2-exon3 of *Lpl*-201 (ENSMUST00000015712.14) transcript is recommended as the knockout region. The region contains 341bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Lpl* 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 targeted null mutations become cyanotic and die within 2 days of birth due to chylomicron engorgement of capillaries. Mutants show hypertriglyceridemia and reduced fat stores. Heterozygotes show 1.5-2-fold elevated triglyceride levels.
- The *Lpl* 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)

Lpl lipoprotein lipase [Mus musculus (house mouse)]

Gene ID: 16956, updated on 19-Mar-2019

Summary



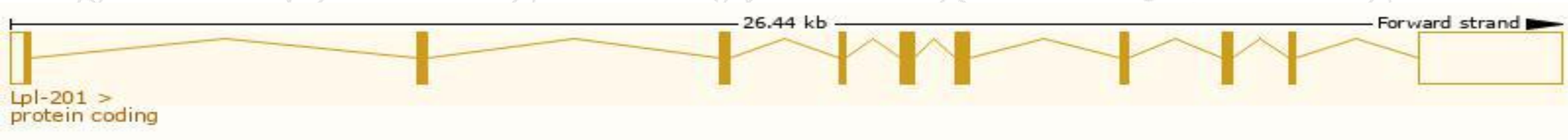
Official Symbol	Lpl provided by MGI
Official Full Name	lipoprotein lipase provided by MGI
Primary source	MGI:MGI:96820
See related	Ensembl:ENSMUSG00000015568
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Expression	Biased expression in subcutaneous fat pad adult (RPKM 870.9), genital fat pad adult (RPKM 464.3) and 3 other tissues See more
Orthologs	human all

Transcript information (Ensembl)

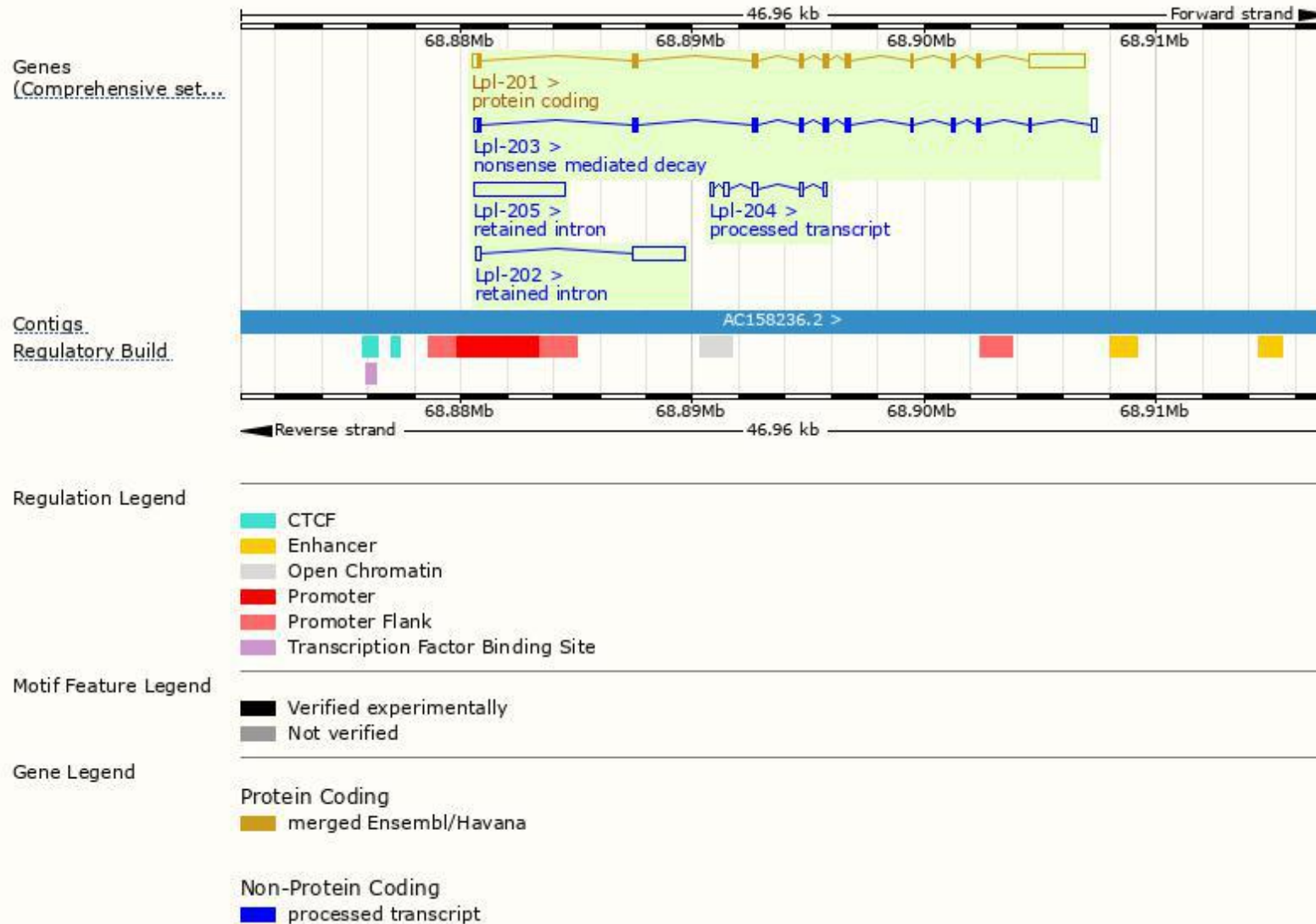
The gene has 5 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Lpl-201	ENSMUST00000015712.14	4115	474aa	Protein coding	CCDS40357	P11152	TSL:1 GENCODE basic APPRIS P1
Lpl-203	ENSMUST00000168401.1	1900	474aa	Nonsense mediated decay	-	P11152	TSL:1
Lpl-204	ENSMUST00000169749.1	851	No protein	Processed transcript	-	-	TSL:3
Lpl-205	ENSMUST00000213071.1	3954	No protein	Retained intron	-	-	TSL:NA
Lpl-202	ENSMUST00000101463.2	2423	No protein	Retained intron	-	-	TSL:1

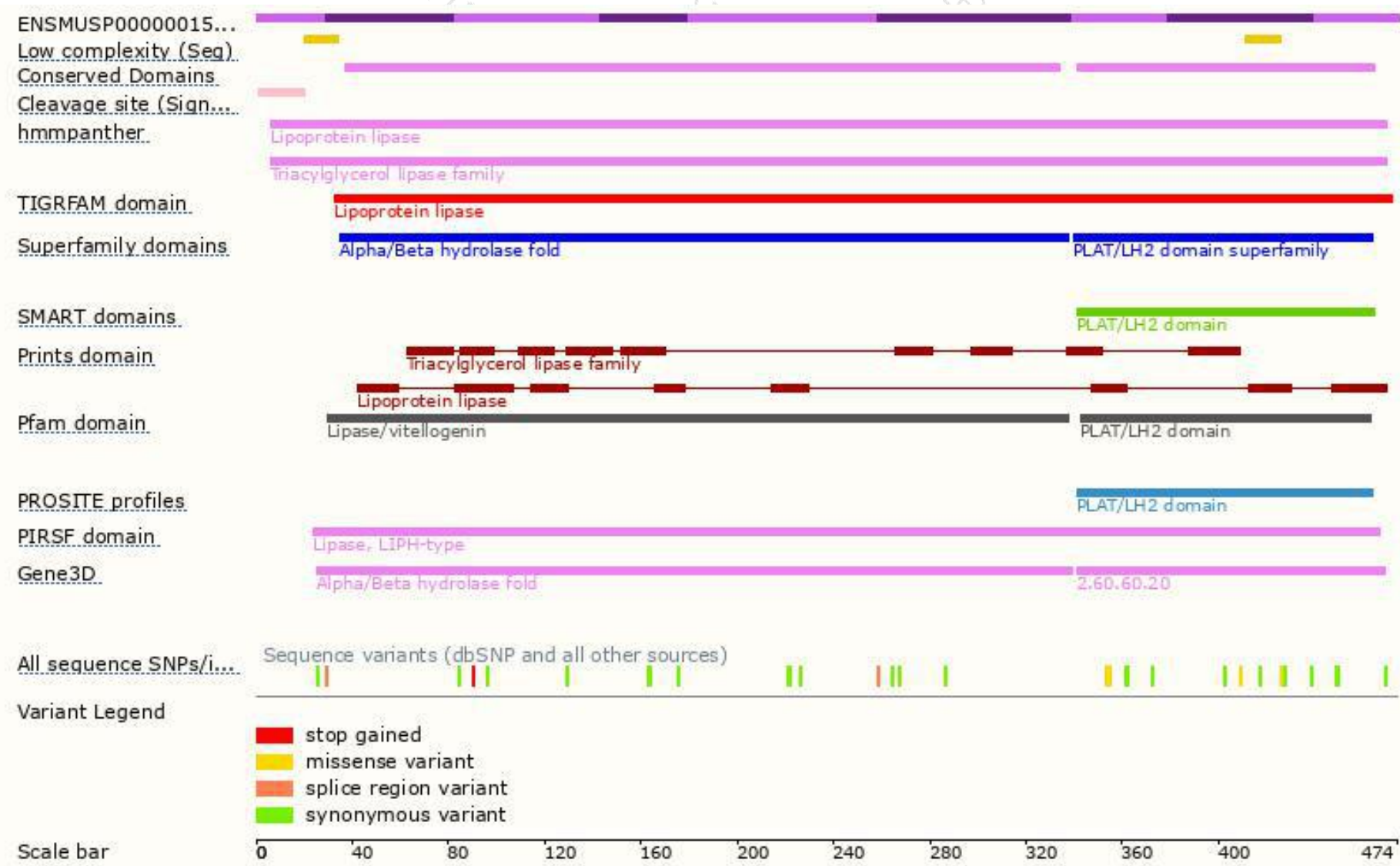
The strategy is based on the design of *Lpl-201* transcript,The transcription is shown below



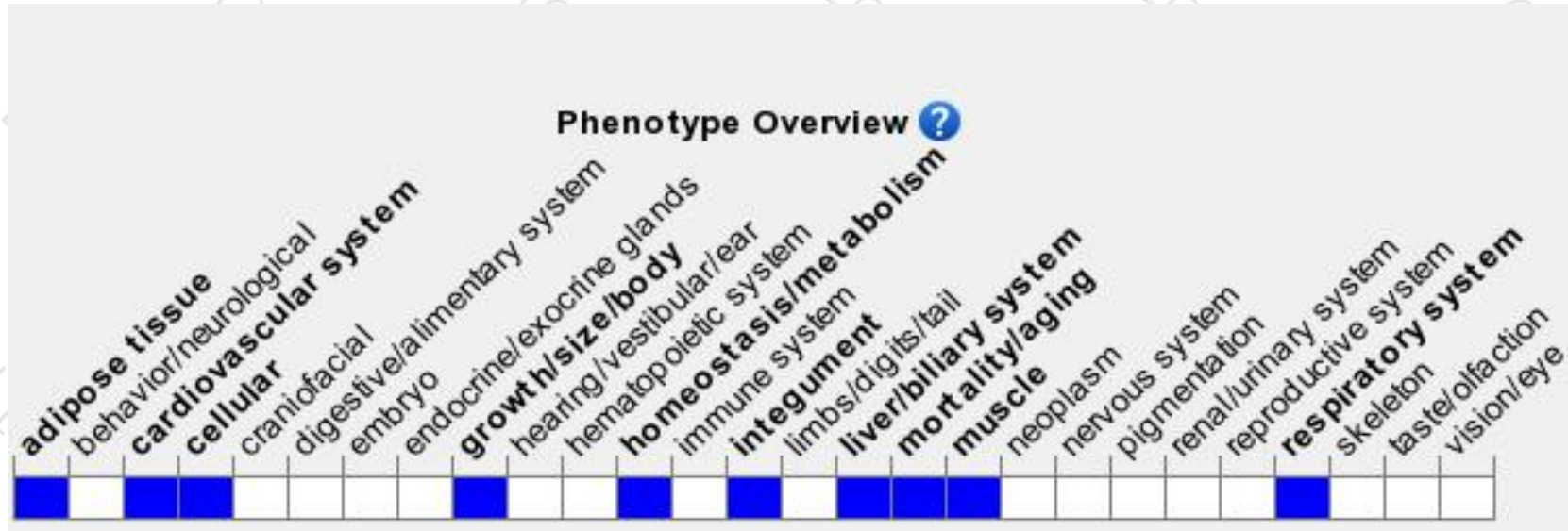
Genomic location distribution



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 targeted null mutations become cyanotic and die within 2 days of birth due to chylomicron engorgement of capillaries. Mutants show hypertriglyceridemia and reduced fat stores.

Heterozygotes show 1.5-2-fold elevated triglyceride levels.

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

Tel: 400-9660890

