Tbl1xr1 Cas9-CKO Strategy

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Project Overview

Project Name	***Tbl1xr1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

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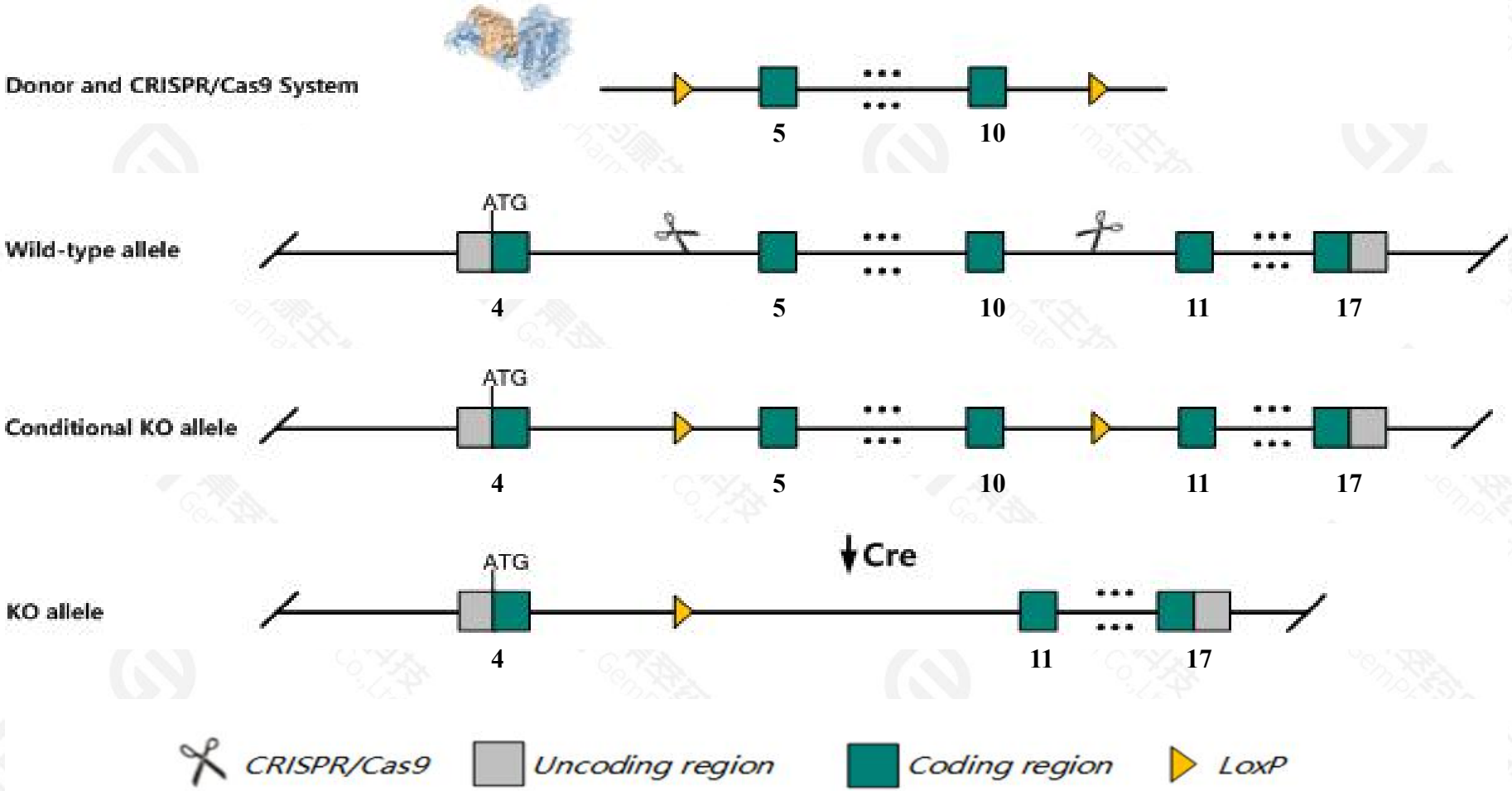
This model will use CRISPR/Cas9 technology to edit the *Tbl1xr1* gene. The schematic diagram is as follows:



Technical routes

➢ The *Tbl1xr1* gene has 11 transcripts. According to the structure of *Tbl1xr1* gene, exon5-exon10 of *Tbl1xr1-203*(ENSMUST00000193734.6) transcript is recommended as the knockout region.The region contains 806bp coding sequence. Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Tbl1xr1* gene. The brief process is as follows:gRNA was transcribed in vitro, donor was constructed.Cas9, gRNA 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.

Notice

➢ According to the existing MGI data,mice homozygous for a conditional allele activated in adipose tissue exhibit increased body weight, and total body fat and increased susceptibility to diet-induced obesity and impaired glucose homeostasis.

➢ Transcript *Tbl1xr1-206* may not be affected.

➢ The *Tbl1xr1* gene is located on the Chr3. 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）

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Tbl1xr1 transducin (beta)-like 1X-linked receptor 1 [Mus musculus (house mouse)]

Gene ID: 81004, updated on 31-Jan-2019

Summary

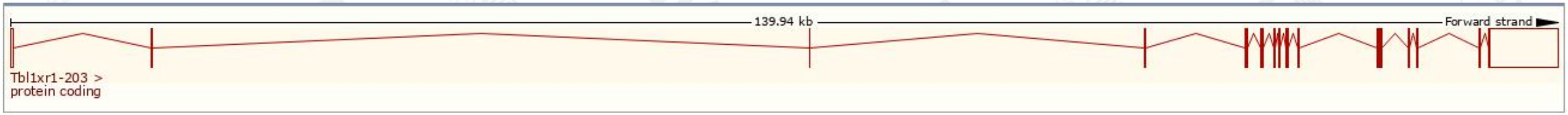
Official Symbol	Tbl1xr1 provided by MGI
Official Full Name	transducin (beta)-like 1X-linked receptor 1 provided by MGI
Primary source	MGI:MGI:2441730
See related	Ensembl:ENSMUSG00000027630
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	8030499H02Rik, A630076E03Rik, AW539987, C21, C230089I12Rik, DC42, Ira1, TBLR1
Expression	Ubiquitous expression in frontal lobe adult (RPKM 4.6), limb E14.5 (RPKM 4.3) and 28 other tissues See more
Orthologs	human all

Transcript information（Ensembl）

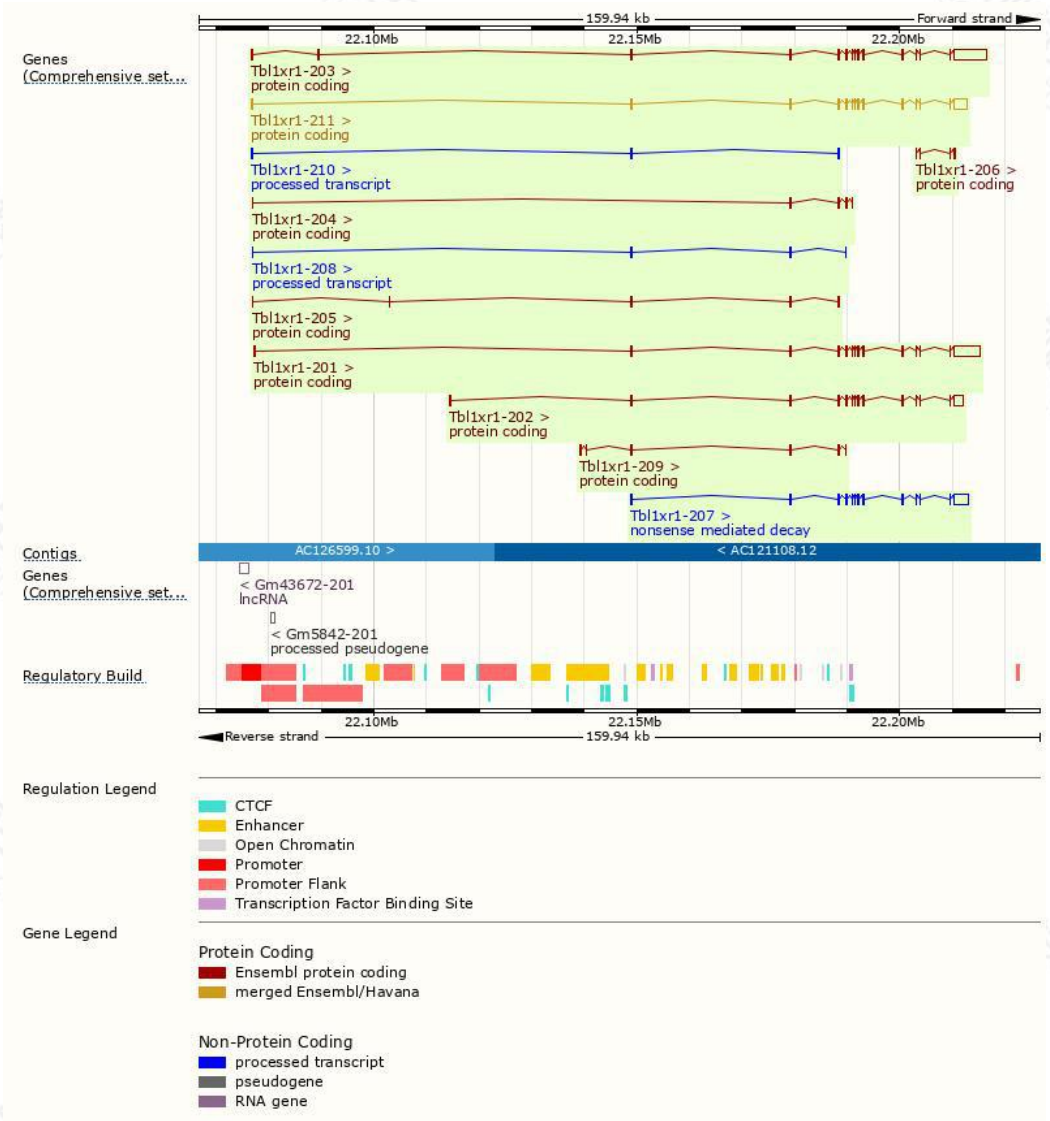
The gene has 11 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Tbl1xr1-203	ENSMUST00000193734.5	8237	514aa	Protein coding	CCDS17266	Q8BHJ5	TSL:1 GENCODE basic APPRIS P1
Tbl1xr1-201	ENSMUST00000063988.13	6667	514aa	Protein coding	CCDS17266	Q8BHJ5	TSL:1 GENCODE basic APPRIS P1
Tbl1xr1-211	ENSMUST00000202747.3	4209	514aa	Protein coding	CCDS17266	Q8BHJ5	TSL:1 GENCODE basic APPRIS P1
Tbl1xr1-202	ENSMUST00000192328.4	3323	514aa	Protein coding	CCDS17266	Q8BHJ5	TSL:1 GENCODE basic APPRIS P1
Tbl1xr1-209	ENSMUST00000202356.3	651	74aa	Protein coding	-	A0A0J9YUR3	CDS 3' incomplete TSL:5
Tbl1xr1-204	ENSMUST00000200793.3	602	144aa	Protein coding	-	A0A0J9YUE3	CDS 3' incomplete TSL:5
Tbl1xr1-205	ENSMUST00000200943.3	376	54aa	Protein coding	-	A0A0J9YVC9	CDS 3' incomplete TSL:5
Tbl1xr1-206	ENSMUST00000201467.1	354	67aa	Protein coding	-	A0A0J9YUT9	CDS 5' incomplete TSL:5
Tbl1xr1-207	ENSMUST00000201509.1	4301	474aa	Nonsense mediated decay	-	A0A0J9YV90	TSL:5
Tbl1xr1-210	ENSMUST00000202647.3	404	No protein	lncRNA	-	-	TSL:5
Tbl1xr1-208	ENSMUST00000202149.3	270	No protein	lncRNA	-	-	TSL:5

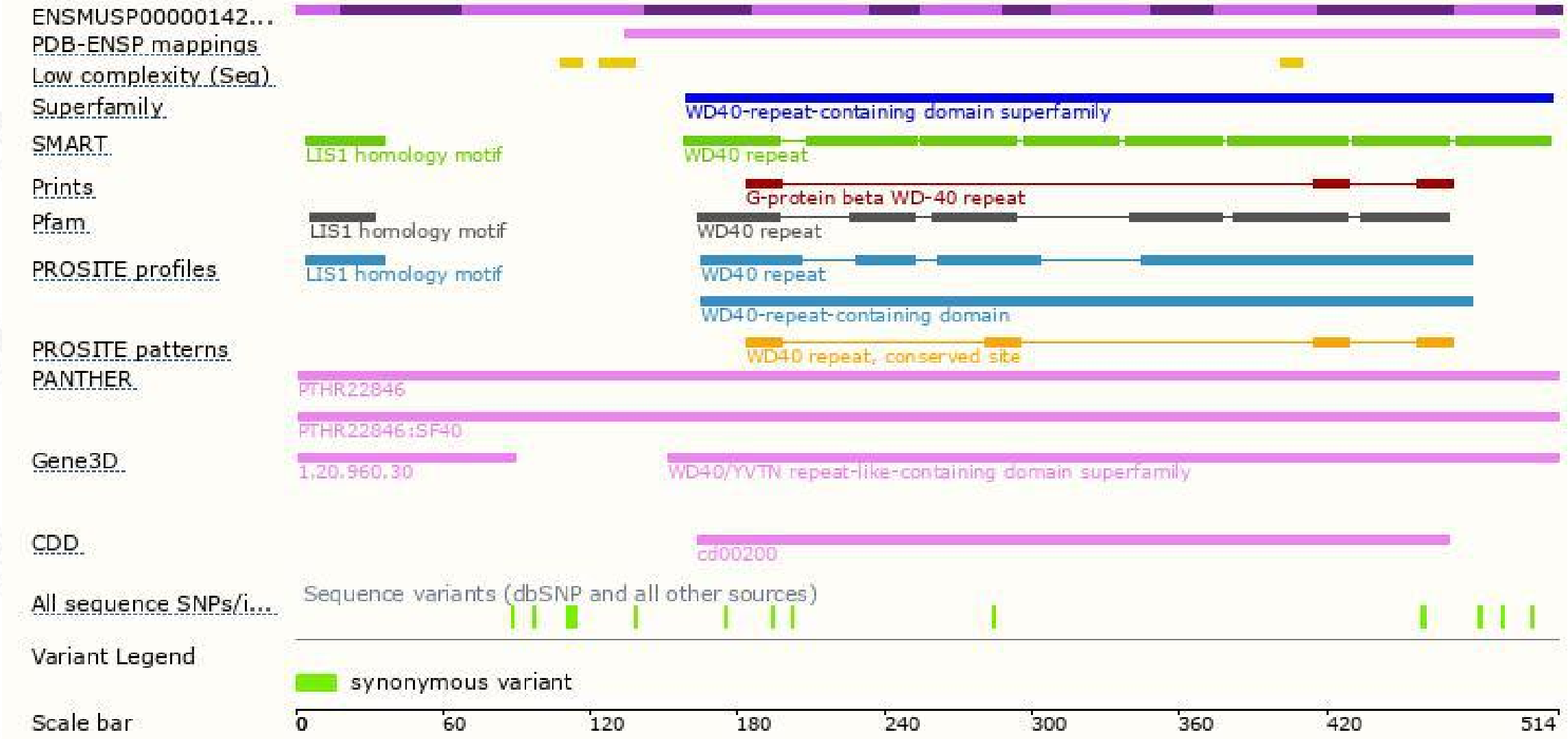
The strategy is based on the design of *Tbl1xr1-203* transcript,the transcription is shown below:



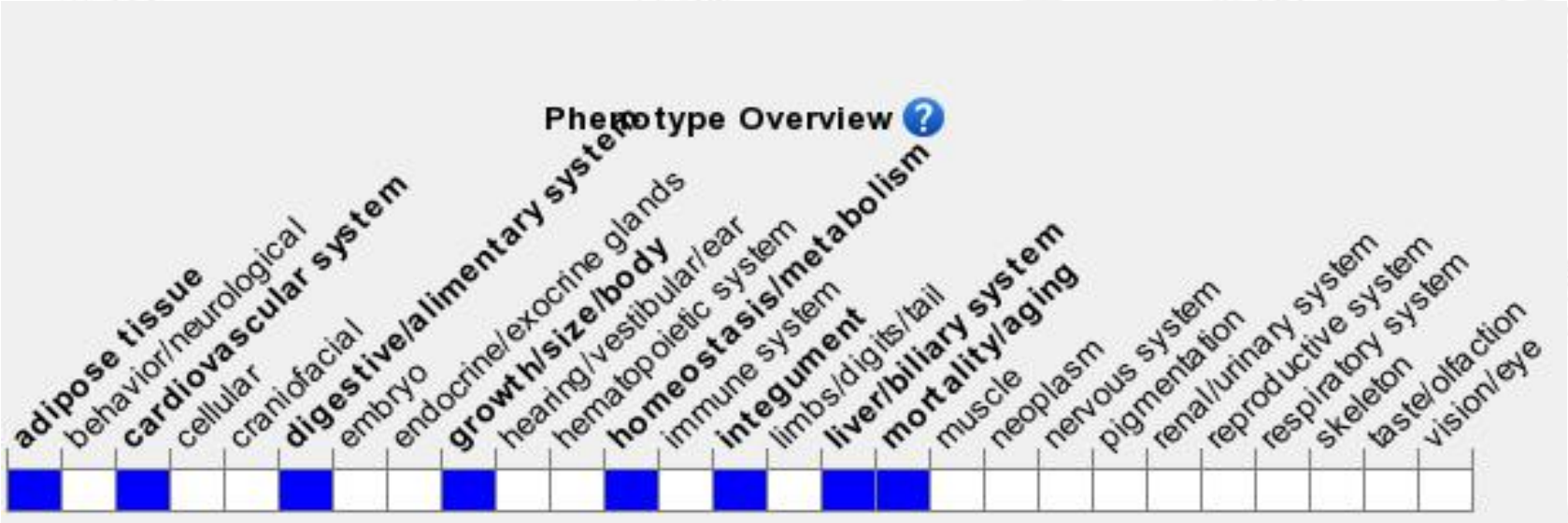
Genomic location distribution



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 conditional allele activated in adipose tissue exhibit increased body weight, and total body fat and increased susceptibility to diet-induced obesity and impaired glucose homeostasis.

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