Ppargc1a Cas9-CKO Strategy

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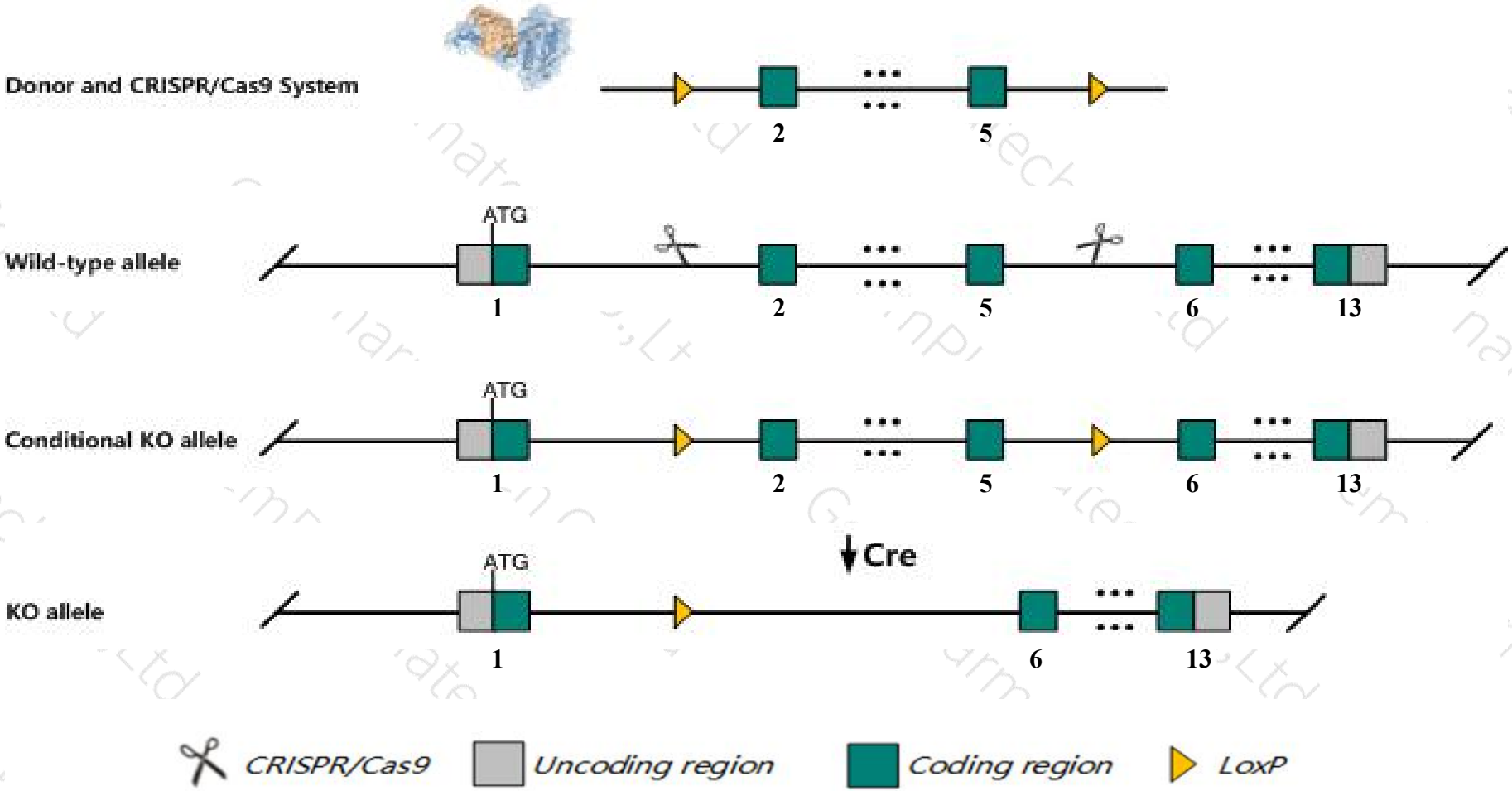
Project Overview

Project Name	***Ppargc1a***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Ppargc1a* gene. The schematic diagram is as follows:



Technical routes

- The *Ppargc1a* gene has 5 transcripts. According to the structure of *Ppargc1a* gene, exon2-exon5 of *Ppargc1a-203* (ENSMUST00000132734.7) transcript is recommended as the knockout region.The region contains 706bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Ppargc1a* 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.

Notice

- According to the existing MGI data,Homozygous null mice display partial postnatal lethality, abnormal glucose and insulin homeostasis, resistance to diet induced obesity, increased oxygen consumption, spongiform encephalopathy, hyperactivity, increased startle reflex, and limb grasping.

- The *Ppargc1a* gene is located on the Chr5. 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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Ppargc1a peroxisome proliferative activated receptor, gamma, coactivator 1 alpha [Mus musculus (house mouse)]

Gene ID: 19017, updated on 9-Apr-2019

Summary

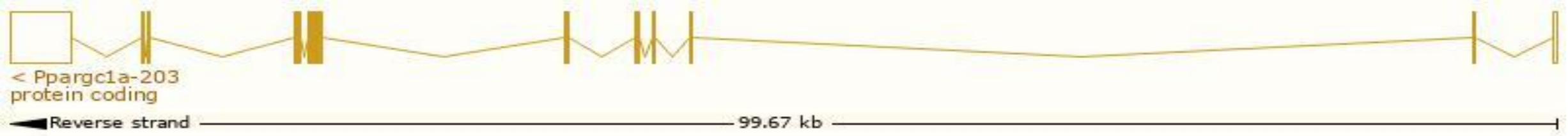
Official Symbol	Ppargc1a provided by MGI
Official Full Name	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha provided by MGI
Primary source	MGI:MGI:1342774
See related	Ensembl:ENSMUSG00000029167
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	A830037N07Rik, Gm11133, PGC-1, PPARGC-1-alpha, Pgc-1alpha, Pgc1, Pgco1, Ppargc1
Summary	This gene encodes a transcriptional coactivator that induces and coordinates gene expression regulating mitochondrial biogenesis, respiration, hepatic gluconeogenesis, thermogenic program in brown fat and muscle fiber-type switching. Mice lacking the encoded protein exhibit reduced thermogenic capacity, hyperactivity and resistance to diet-induced obesity. Mice lacking the encoded protein specifically in the heart exhibit peripartum cardiomyopathy. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Sep 2015]
Expression	Broad expression in heart adult (RPKM 4.1), frontal lobe adult (RPKM 3.9) and 22 other tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

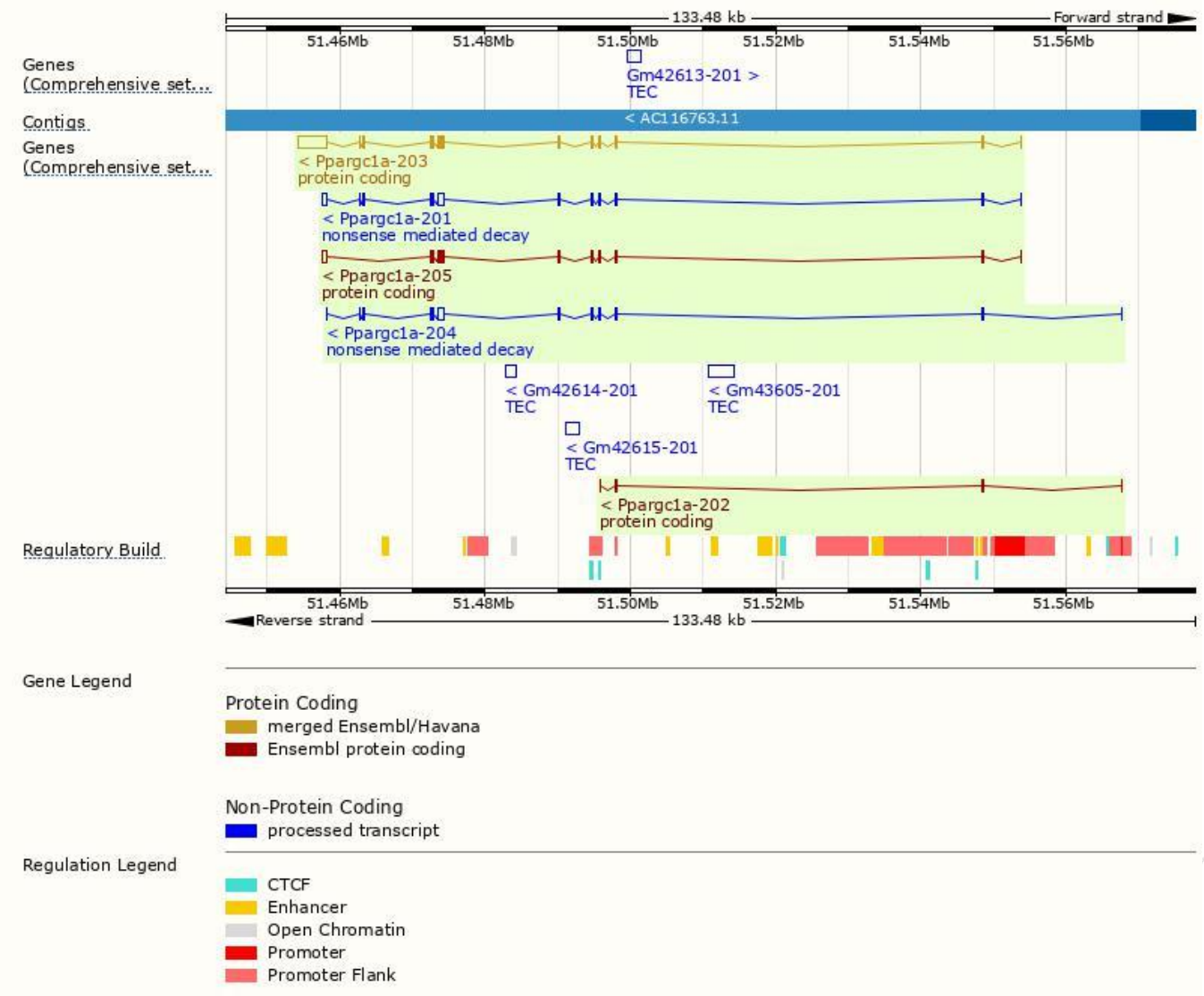
The gene has 5 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Ppargc1a-203	ENSMUST00000132734.7	6464	797aa	Protein coding	CCDS19282	O70343	TSL:1 GENCODE basic APPRIS P1
Ppargc1a-205	ENSMUST00000196968.4	2754	696aa	Protein coding	-	A0A0G2JGG3	TSL:5 GENCODE basic
Ppargc1a-202	ENSMUST00000127135.2	488	142aa	Protein coding	-	D3YZS8	CDS 3' incomplete TSL:5
Ppargc1a-201	ENSMUST00000031059.13	3041	270aa	Nonsense mediated decay	-	Q3LIG2	TSL:1
Ppargc1a-204	ENSMUST00000151104.7	2452	266aa	Nonsense mediated decay	-	O70343	TSL:1

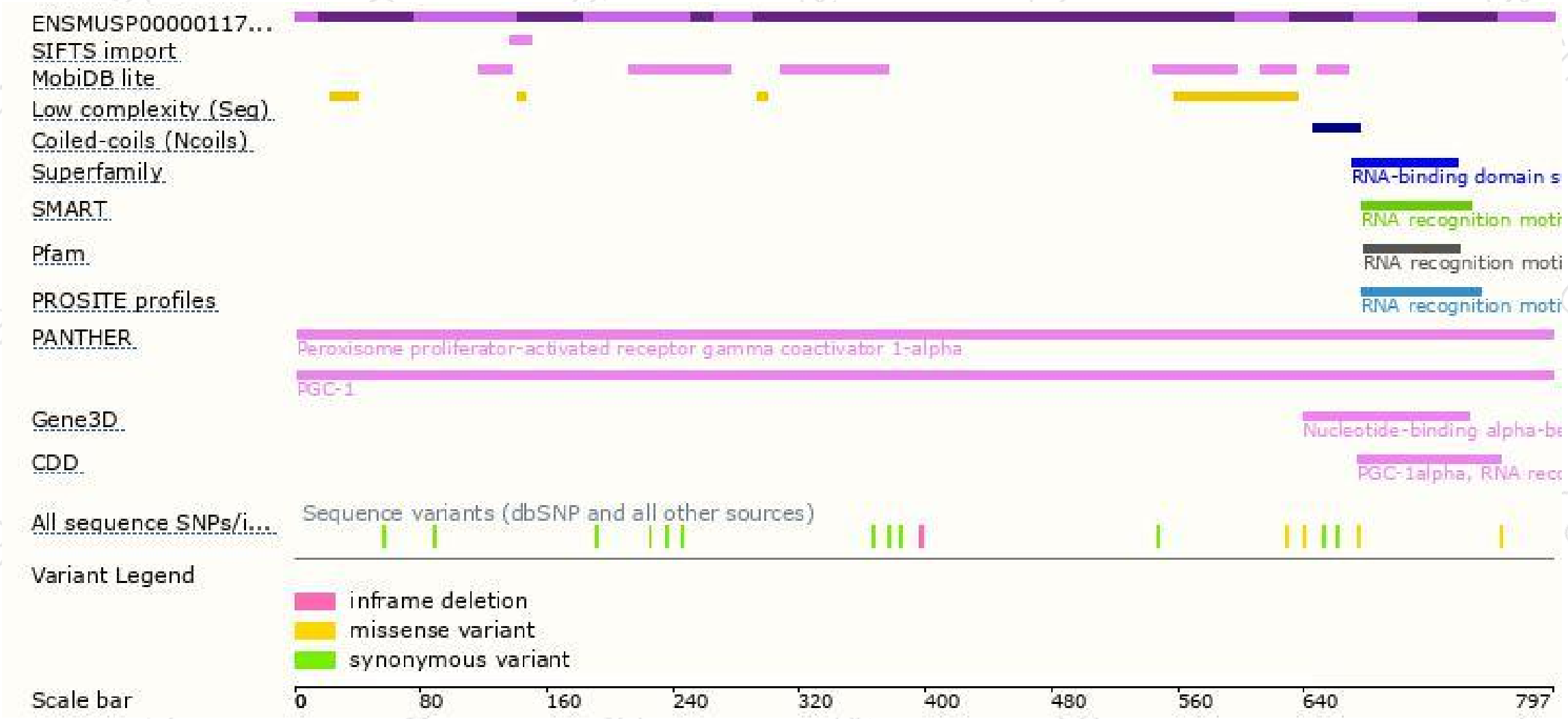
The strategy is based on the design of *Ppargc1a-203* transcript,The transcription is shown below



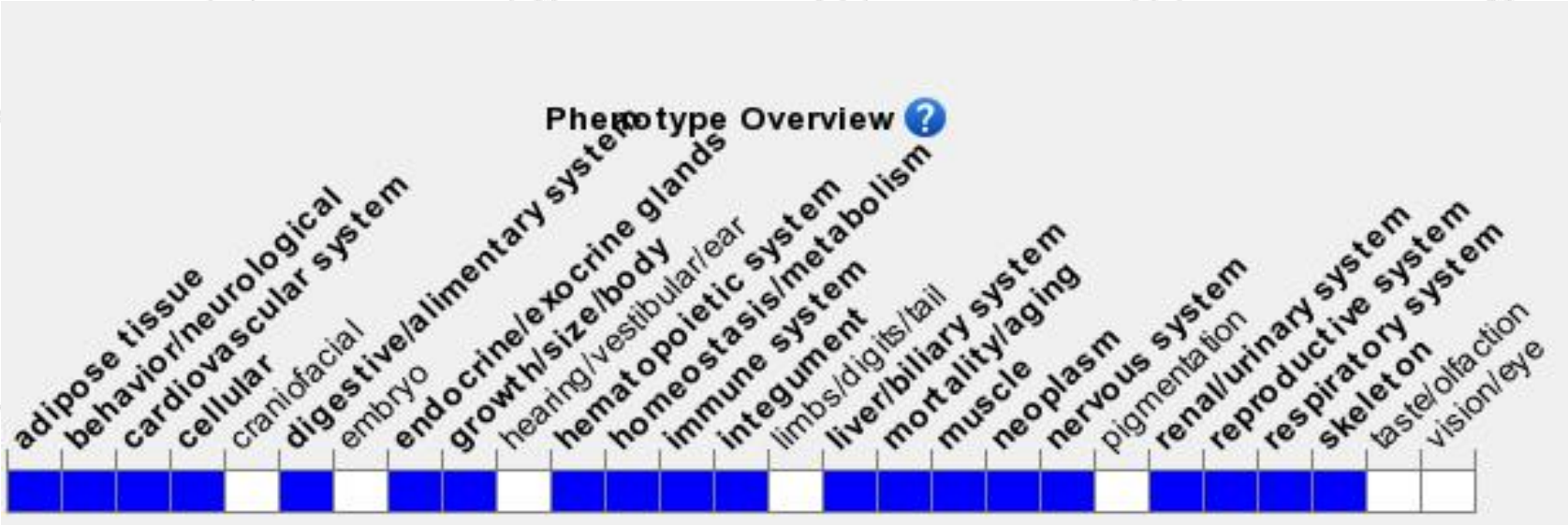
Genomic location distribution



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/).

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

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