Hexa Cas9-KO Strategy

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Reviewer: Jia Yu

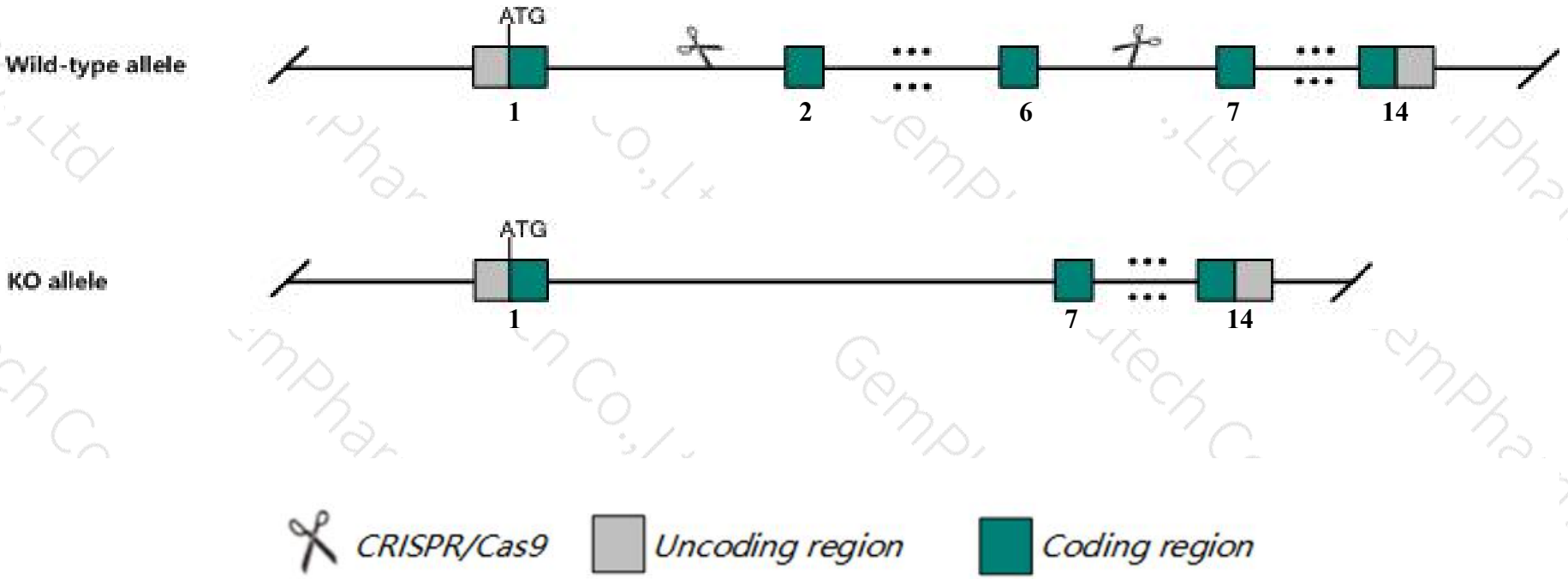
Design Date: 2020-2-10

Project Overview

Project Name	***Hexa***
Project type	**Cas9-KO**
Strain background	**C57BL/6JGpt**

Knockout strategy

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



Technical routes

➢ The *Hexa* gene has 1 transcript. According to the structure of *Hexa* gene, exon2-exon6 of *Hexa-201* (ENSMUST00000026262.7) transcript is recommended as the knockout region.The region contains 419bp coding sequence. Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Hexa* gene. The brief process is as follows: CRISPR/Cas9 system

Notice

- According to the existing MGI data,Homozygous mutants accumulate excess amounts of GM2 ganglioside that is stored in neurons as membranous cytoplasmic bodies typically seen in the neurons of Tay-Sachs disease patients. However, the mutant mice appear to be functionally normal.

- The *Hexa* gene is located on the Chr9. 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 the gene knockout on gene transcription, RNA splicing and protein translation cannot be predicted at the existing technology level.

Gene information（NCBI）

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Hexa hexosaminidase A [Mus musculus (house mouse)]

Gene ID: 15211, updated on 31-Jan-2019

Summary

Official Symbol	Hexa provided by MGI
Official Full Name	hexosaminidase A provided by MGI
Primary source	MGI:MGI:96073
See related	Ensembl:ENSMUSG00000025232
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	Hex-1
Summary	This gene encodes a member of the glycosyl hydrolase 20 family of proteins. The encoded preproprotein is proteolytically processed to generate the alpha subunit of the lysosomal enzyme beta-hexosaminidase. This enzyme, together with the cofactor GM2 activator protein, catalyzes the degradation of the ganglioside GM2, and other molecules containing terminal N-acetyl hexosamines. Mice lacking the encoded protein exhibit accumulation of gangliosides in the brain and membranous cytoplasmic bodies in neurons. Certain mutations in the human ortholog of this gene cause Tay-Sachs disease. [provided by RefSeq, Aug 2016]
Expression	Ubiquitous expression in placenta adult (RPKM 87.6), colon adult (RPKM 64.8) and 28 other tissuesSee more
Orthologs	human all

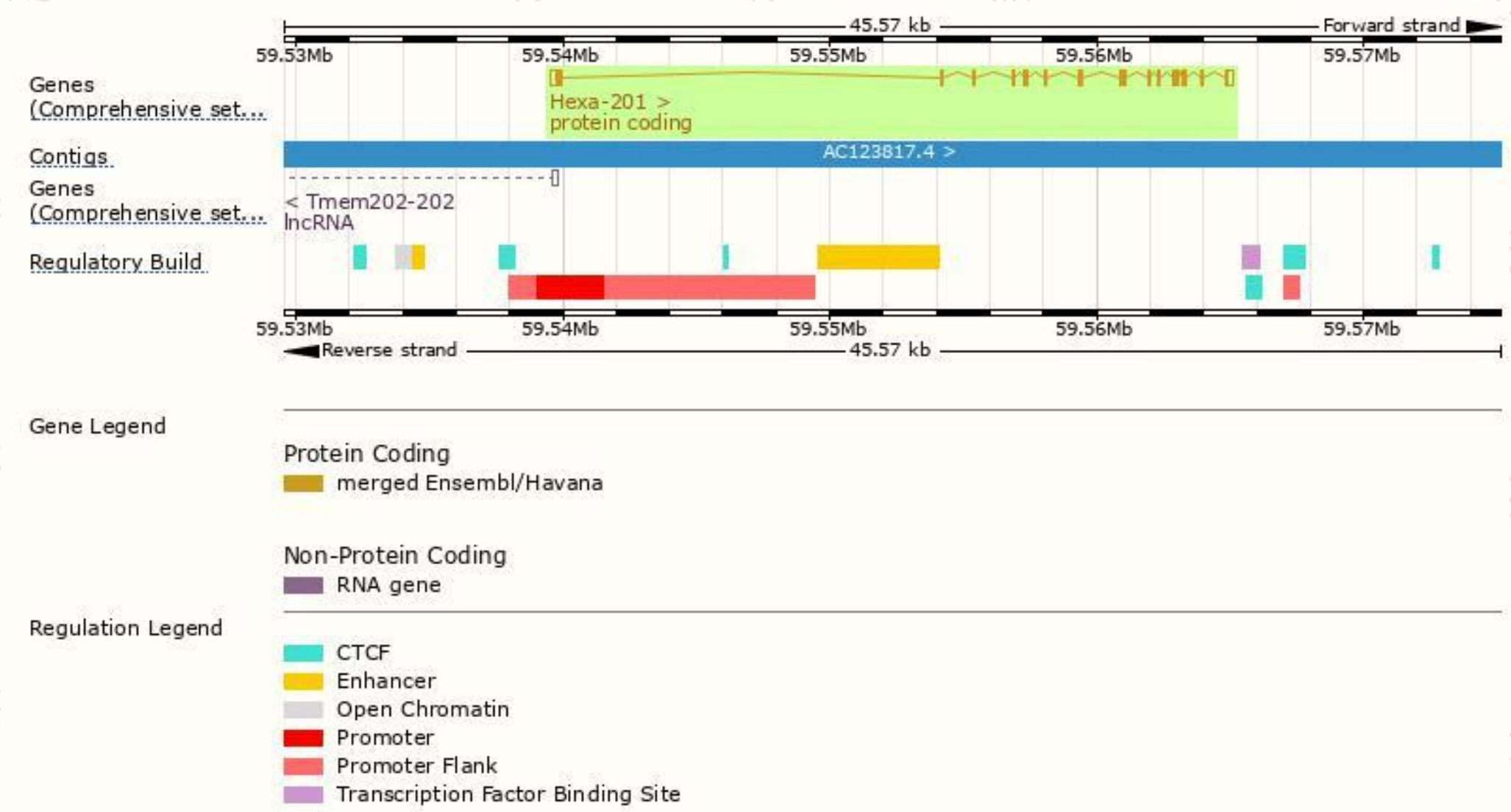
Transcript information（Ensembl）

The gene has 1 transcript,and the transcript is shown below:

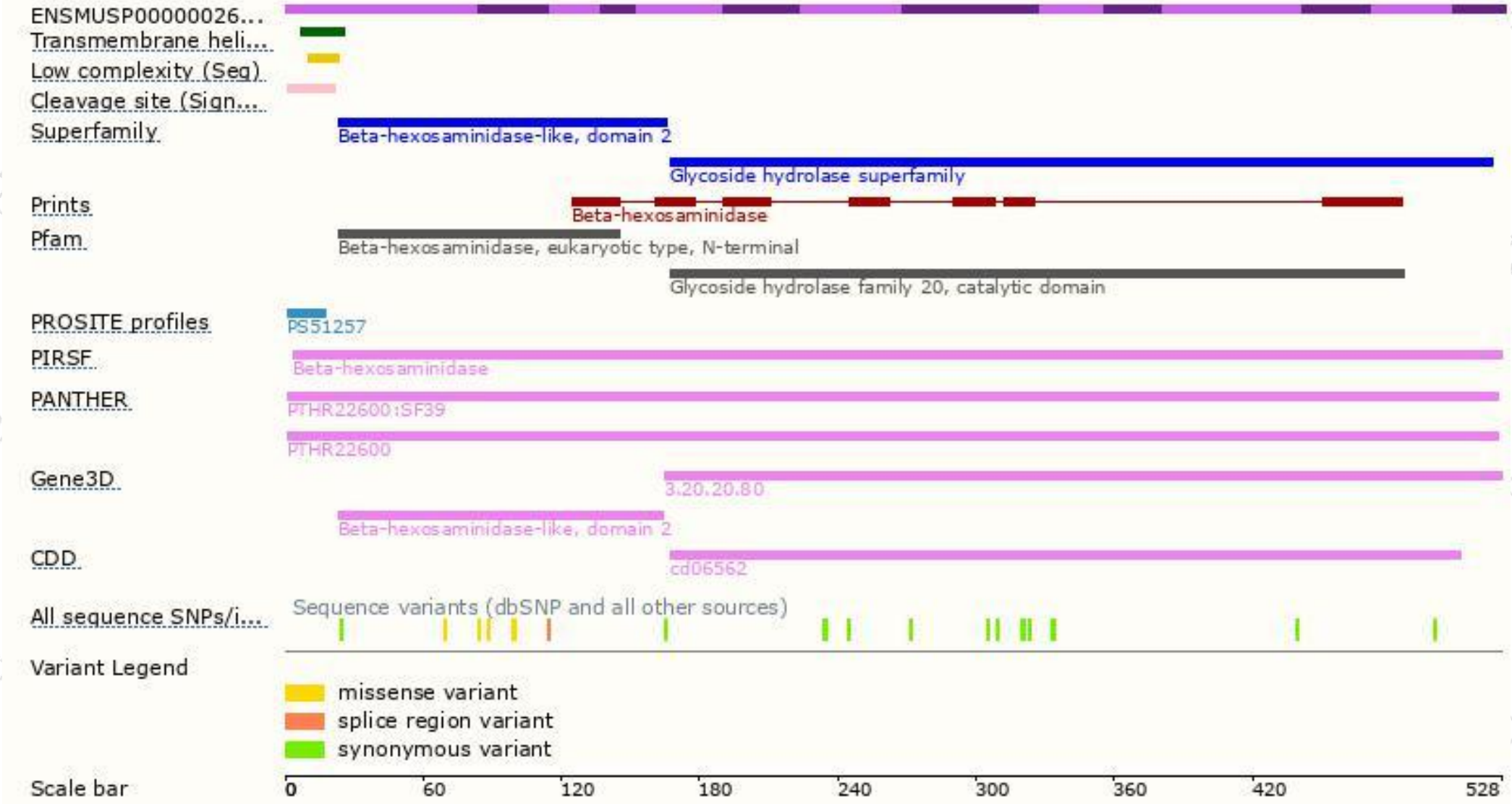
Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Hexa-201	ENSMUST00000026262.7	1996	528aa	Protein coding	CCDS23250	P29416	TSL:1 GENCODE basic APPRIS P1

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

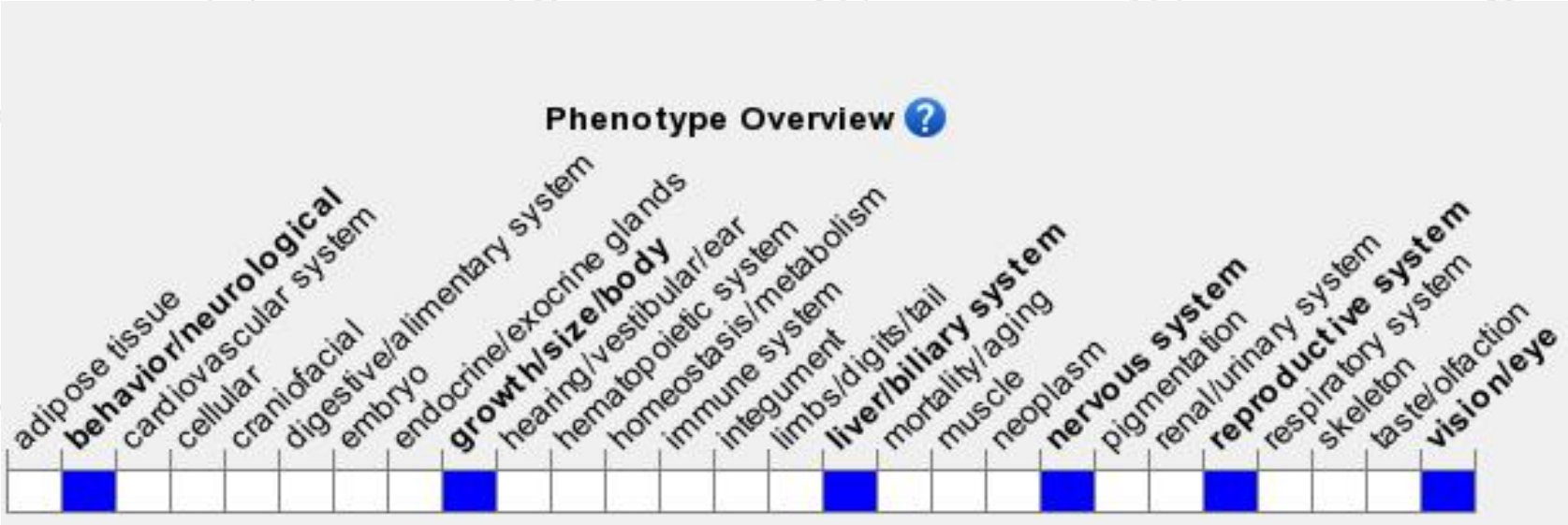
Genomic location distribution



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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