Syngap1 Cas9-CKO Strategy

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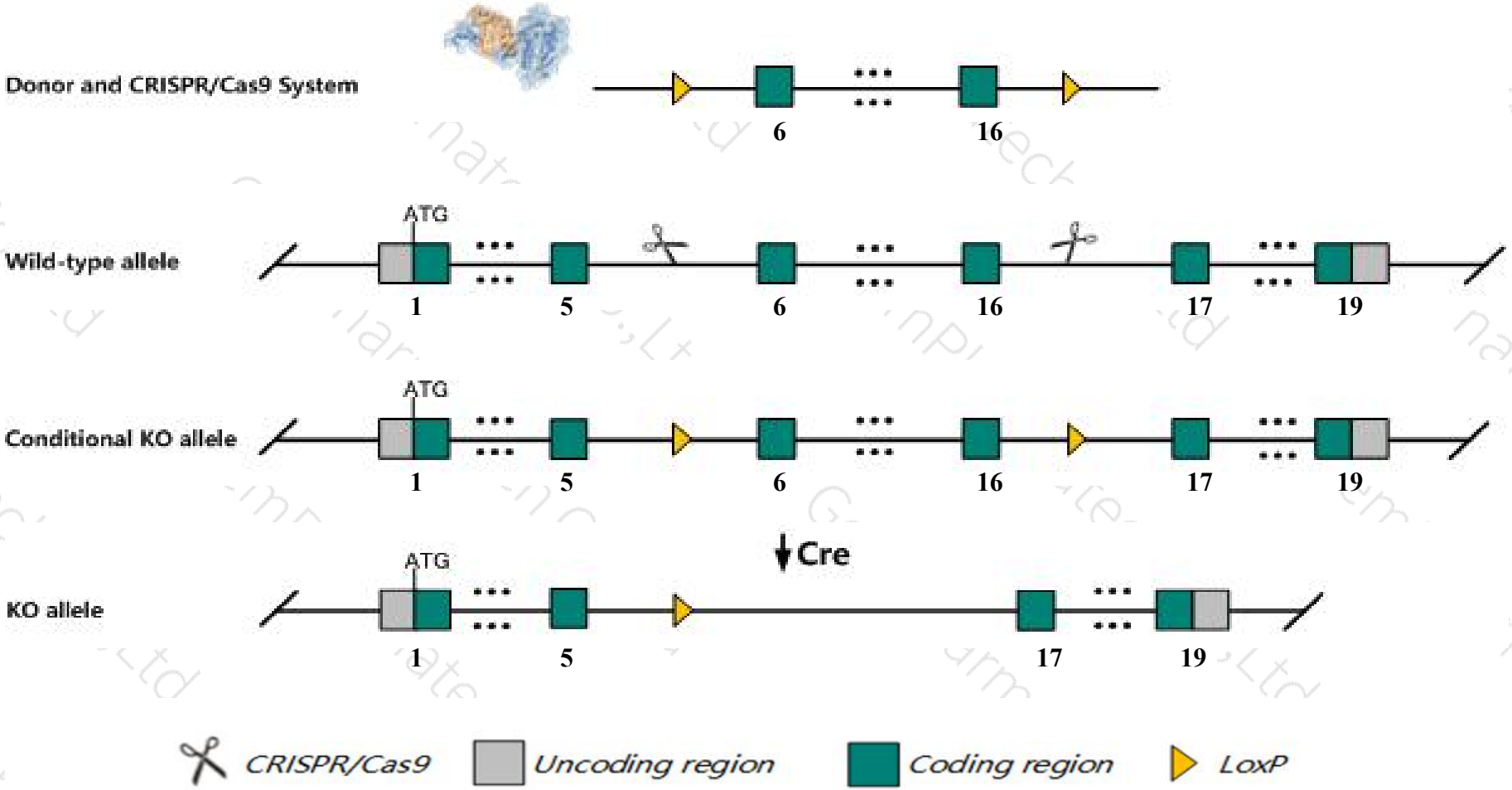
Project Overview

Project Name	***Syngap1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Syngap1* gene. The schematic diagram is as follows:



Technical routes

- The *Syngap1* gene has 14 transcripts. According to the structure of *Syngap1* gene, exon6-exon16 of *Syngap1-204* (ENSMUST00000194598.5) transcript is recommended as the knockout region.The region contains 3064bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Syngap1* 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 mutant mice exhibit postnatal lethality, and by P3-P4, exhibit small body size and brain, reduced movement and do not feed.

- The *Syngap1* gene is located on the Chr17. 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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Syngap1 synaptic Ras GTPase activating protein 1 homolog (rat) [Mus musculus (house mouse)]

Gene ID: 240057, updated on 7-Apr-2019

Summary

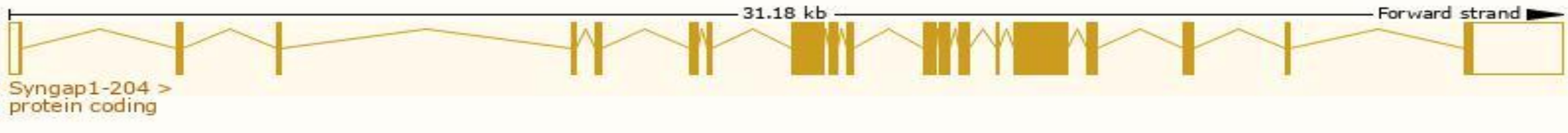
Official Symbol	Syngap1 provided by MGI
Official Full Name	synaptic Ras GTPase activating protein 1 homolog (rat) provided by MGI
Primary source	MGI:MGI:3039785
See related	Ensembl:ENSMUSG00000067629
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	Gm1963, Syngap
Summary	This gene encodes a Ras GTPase activating protein that is a member of the N-methyl-D-aspartate receptor complex. The N-terminal domain of the protein contains a Ras-GAP domain, a pleckstrin homology domain, and a C2 domain that may be involved in binding of calcium and phospholipids. The C-terminal domain consists of a ten histidine repeat region, serine and tyrosine phosphorylation sites, and a T/SXV motif required for postsynaptic scaffold protein interaction. The encoded protein negatively regulates Ras, Rap and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor trafficking to the postsynaptic membrane to regulate synaptic plasticity and neuronal homeostasis. Homozygous null mutations result in early post-embryonic lethality, while heterozygous mutant mice display a variety of phenotypes that include learning and memory defects, hyperactivity, and audiogenic seizures. [provided by RefSeq, Nov 2016]
Expression	Broad expression in frontal lobe adult (RPKM 23.1), cortex adult (RPKM 20.3) and 18 other tissues See more
Orthologs	human all

Transcript information（Ensembl）

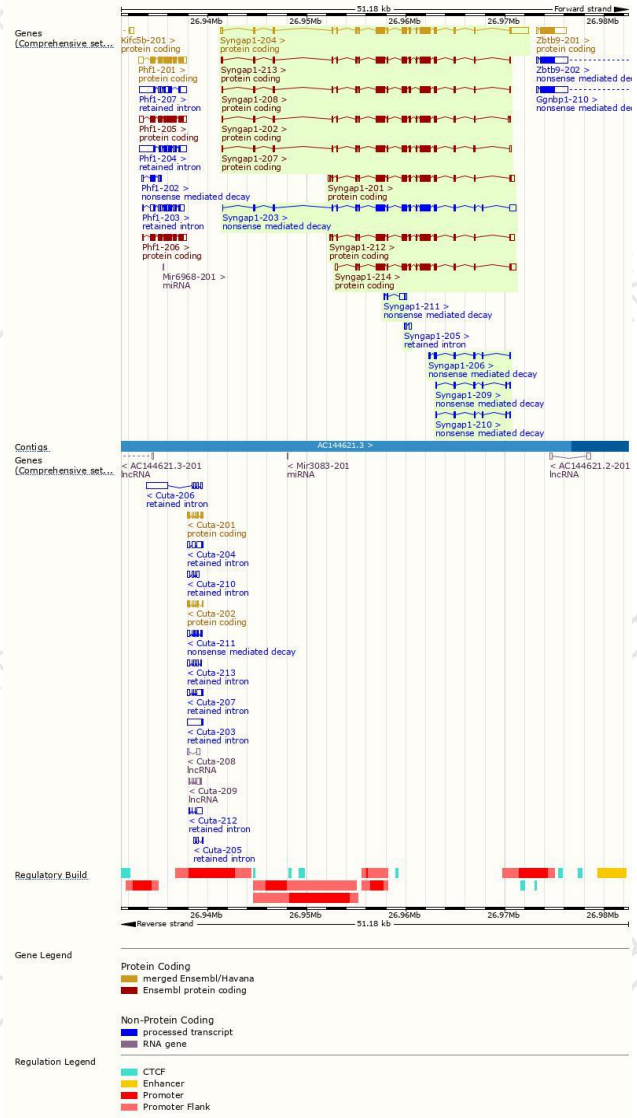
The gene has 14 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Syngap1-204	ENSMUST00000194598.5	6011	1340aa	Protein coding	CCDS59625	F6SEU4	TSL:5 GENCODE basic APPRIS P2
Syngap1-201	ENSMUST00000081285.8	4315	1281aa	Protein coding	-	A0A140T8K9	TSL:5 GENCODE basic APPRIS ALT2
Syngap1-214	ENSMUST00000231853.1	4256	1167aa	Protein coding	-	A0A338P799	GENCODE basic APPRIS ALT2
Syngap1-212	ENSMUST00000228963.1	4133	1246aa	Protein coding	-	A0A2R8VH83	GENCODE basic APPRIS ALT2
Syngap1-207	ENSMUST00000201349.5	4057	1282aa	Protein coding	-	A0A0J9YVH8	CDS 5' incomplete TSL:5
Syngap1-213	ENSMUST00000229490.1	4048	1305aa	Protein coding	-	A0A2R8VHH2	GENCODE basic APPRIS ALT2
Syngap1-202	ENSMUST00000177932.6	3927	1308aa	Protein coding	-	J3QQ18	TSL:5 GENCODE basic APPRIS ALT2
Syngap1-208	ENSMUST00000201702.4	3920	1289aa	Protein coding	-	A0A0J9YUM2	TSL:5 APPRIS ALT2
Syngap1-203	ENSMUST00000193200.5	4532	1281aa	Nonsense mediated decay	-	A0A0A6YVS6	CDS 5' incomplete TSL:5
Syngap1-206	ENSMUST00000201186.3	827	214aa	Nonsense mediated decay	-	A0A0J9YUZ2	CDS 5' incomplete TSL:5
Syngap1-211	ENSMUST00000202939.1	821	65aa	Nonsense mediated decay	-	A0A0J9YUY7	CDS 5' incomplete TSL:5
Syngap1-209	ENSMUST00000202049.3	700	117aa	Nonsense mediated decay	-	A0A0J9YV63	CDS 5' incomplete TSL:5
Syngap1-210	ENSMUST00000202208.1	663	124aa	Nonsense mediated decay	-	A0A0J9YUZ5	CDS 5' incomplete TSL:5
Syngap1-205	ENSMUST00000200799.1	423	No protein	Retained intron	-	-	TSL:3

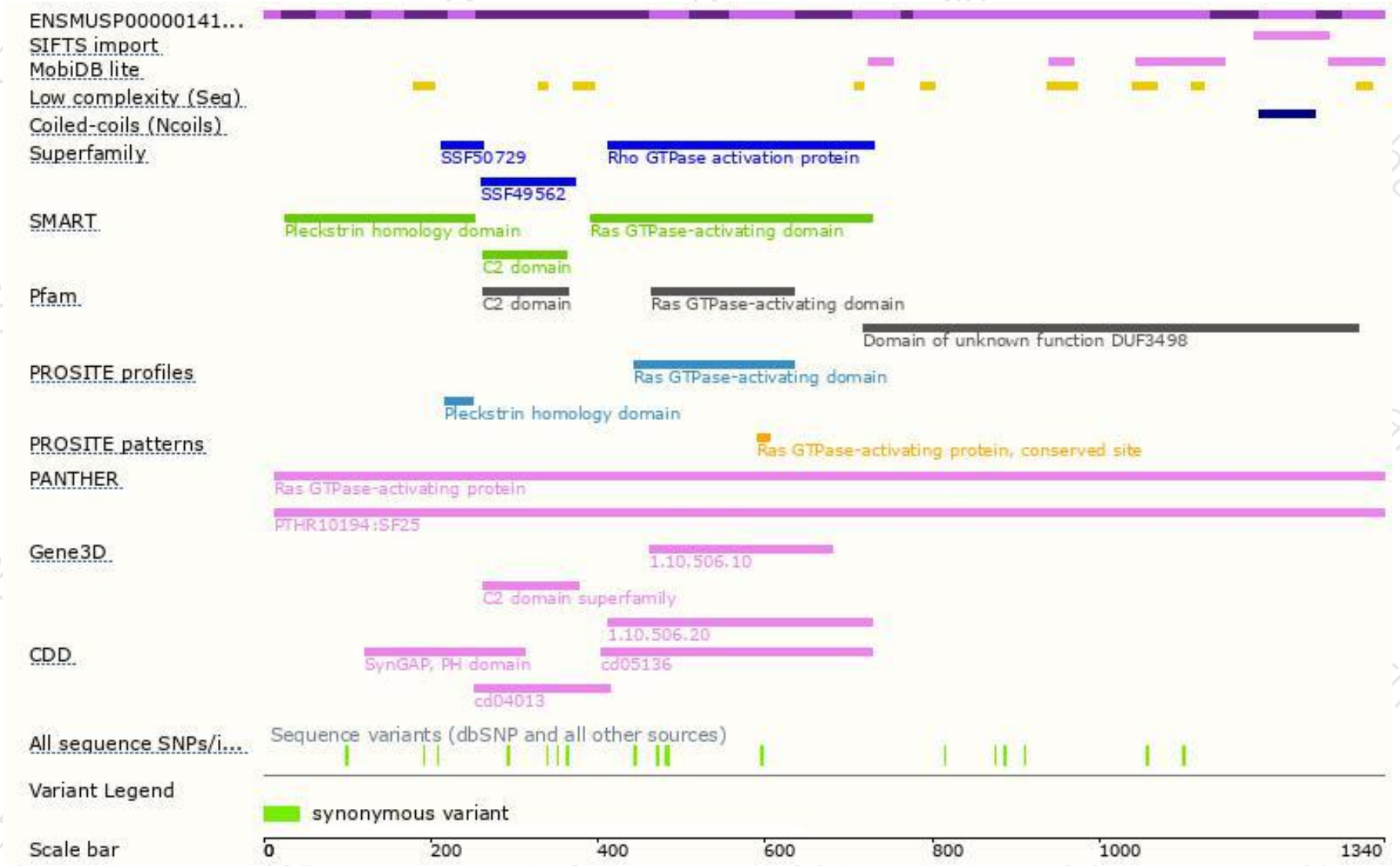
The strategy is based on the design of *Syngap1-204* transcript,The transcription is shown below



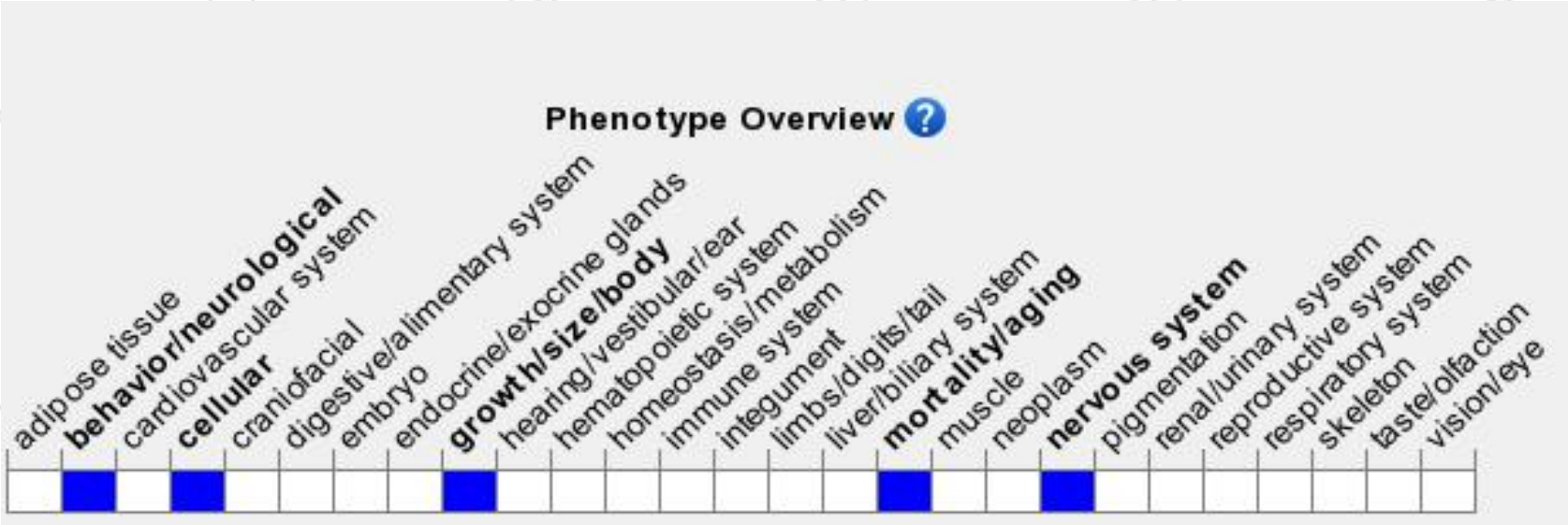
Genomic location distribution



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,Homozygous mutant mice exhibit postnatal lethality, and by P3-P4, exhibit small body size and brain, reduced movement and do not feed.

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

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