

***Nrg1* Cas9-CKO Strategy**

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Project Overview

Project Name

Nrg1

Project type

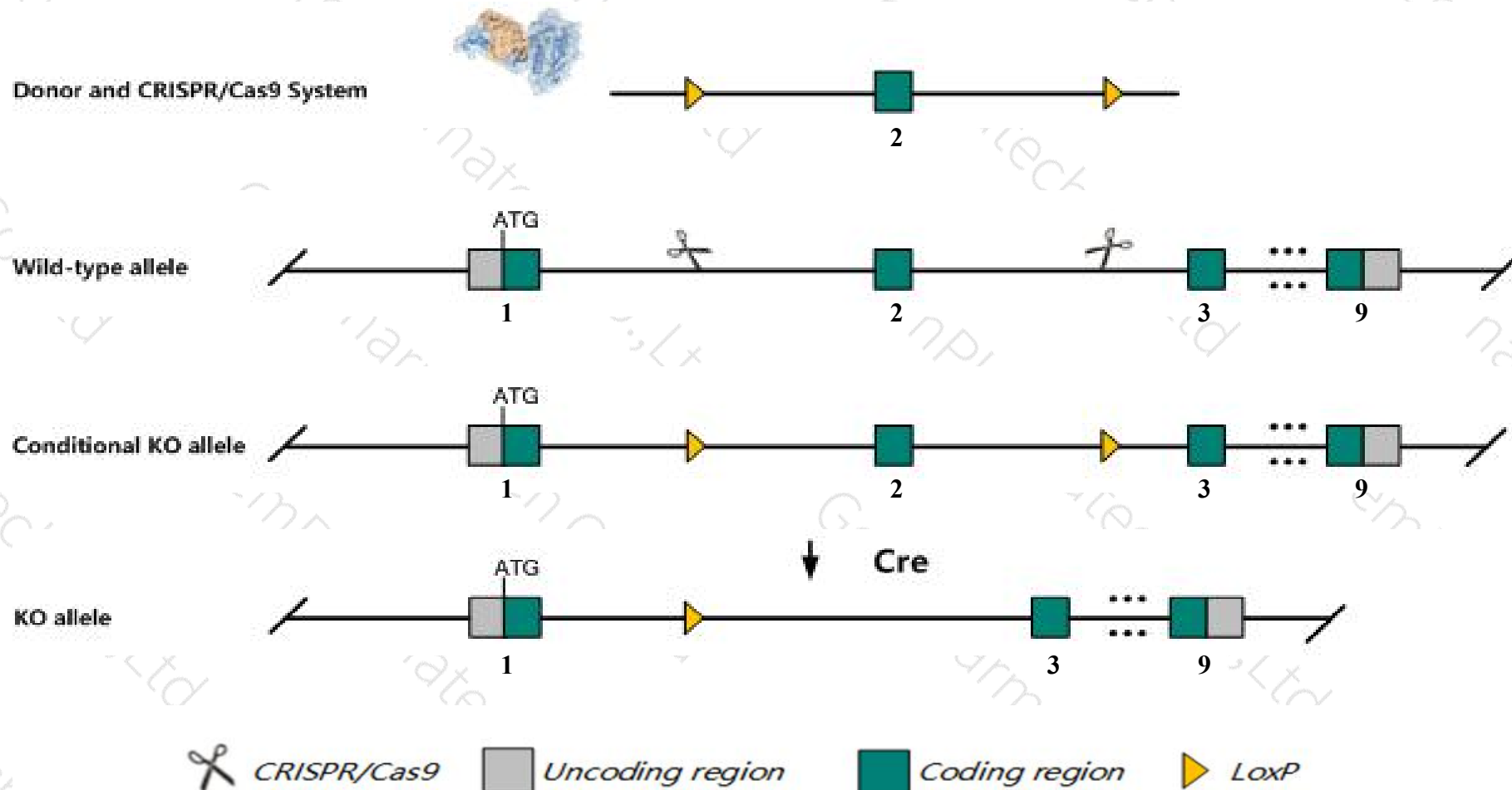
Cas9-CKO

Strain background

C57BL/6JGpt

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Nrg1* gene. The schematic diagram is as follows:



Technical routes

- The *Nrg1* gene has 18 transcripts. According to the structure of *Nrg1* gene, exon2 of *Nrg1-201* (ENSMUST00000073884.5) transcript is recommended as the knockout region. The region contains 130bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Nrg1* 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 exhibit heart defects, impaired development of Schwann cell precursors, cranial ganglia, and radial glia cells, and die at embryonic day 10.5-11.5. Heterozygotes are hyperactive with reduced NMDA receptors.
- The *Nrg1* 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)

Nrg1 neuregulin 1 [Mus musculus (house mouse)]

Gene ID: 211323, updated on 9-Apr-2019

Summary



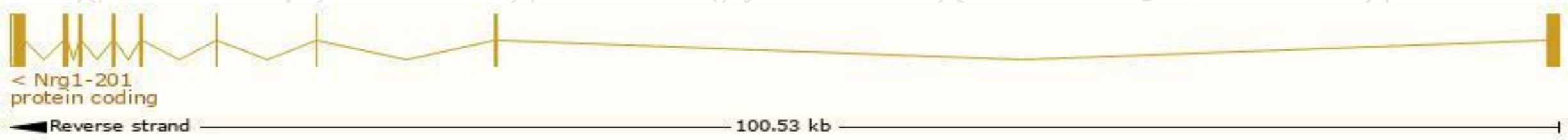
Official Symbol	Nrg1 provided by MGI
Official Full Name	neuregulin 1 provided by MGI
Primary source	MGI:MGI:96083
See related	Ensembl:ENSMUSG00000062991
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	6030402G23Rik, ARIA, D230005F13Rik, GGF, GGFII, HRG, HRGalpha, Hgl, NDF, SMDF
Expression	Broad expression in whole brain E14.5 (RPKM 2.0), CNS E14 (RPKM 1.9) and 17 other tissues See more
Orthologs	human all

Transcript information (Ensembl)

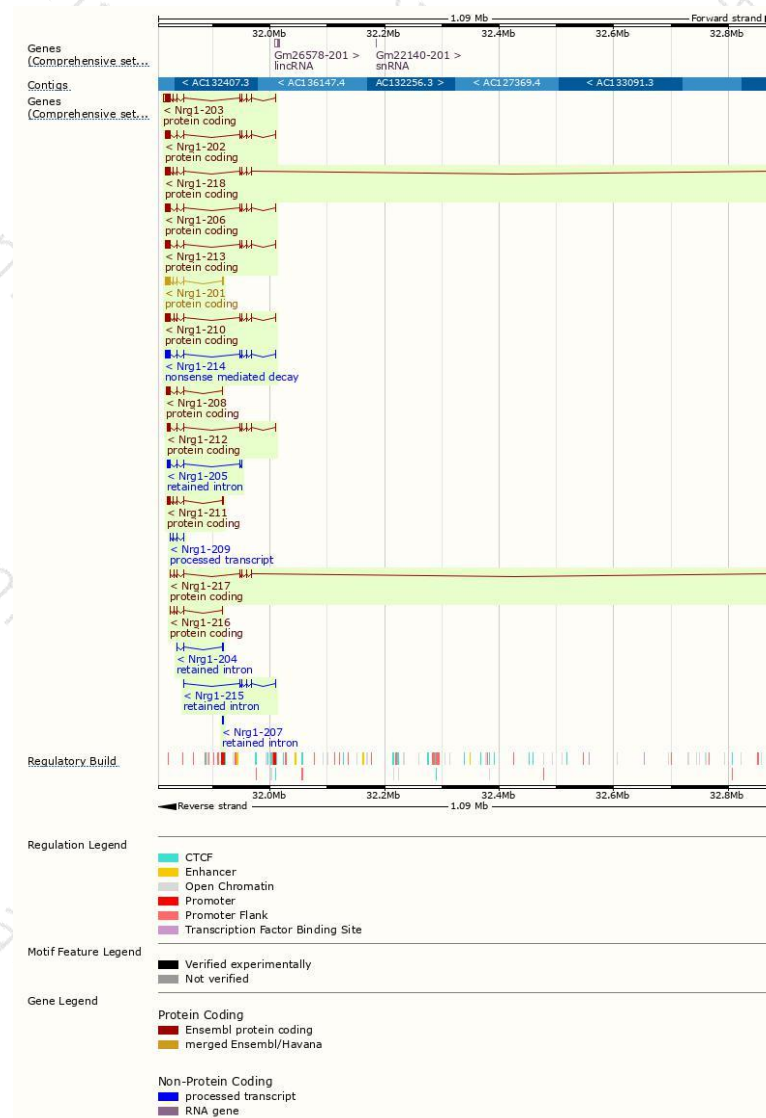
The gene has 18 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Nrg1-201	ENSMUST00000073884.5	2452	700aa	Protein coding	CCDS40315	Q6DR99	TSL:1 GENCODE basic APPRIS P2
Nrg1-203	ENSMUST000000207470.1	5415	645aa	Protein coding	-	Q6DR98	TSL:1 GENCODE basic APPRIS ALT2
Nrg1-202	ENSMUST000000207417.1	3138	637aa	Protein coding	-	A0A140LIP8	TSL:5 GENCODE basic APPRIS ALT2
Nrg1-218	ENSMUST000000209107.1	2972	652aa	Protein coding	-	A0A140LHZ9	TSL:5 GENCODE basic APPRIS ALT2
Nrg1-213	ENSMUST000000208617.1	2787	462aa	Protein coding	-	A0A140LIK5	TSL:5 GENCODE basic
Nrg1-206	ENSMUST000000208205.1	2645	640aa	Protein coding	-	A0A140LJC1	TSL:5 GENCODE basic APPRIS ALT2
Nrg1-210	ENSMUST000000208488.1	2403	663aa	Protein coding	-	A0A140LJ88	TSL:5 GENCODE basic
Nrg1-211	ENSMUST000000208497.1	2096	483aa	Protein coding	-	A0A140LIG9	TSL:1 GENCODE basic
Nrg1-212	ENSMUST000000208598.1	1778	423aa	Protein coding	-	A0A140LHN1	TSL:5 GENCODE basic
Nrg1-217	ENSMUST000000209022.1	1026	266aa	Protein coding	-	A0A140LIJ3	CDS 3' incomplete TSL:5
Nrg1-208	ENSMUST000000208335.1	900	300aa	Protein coding	-	A0A140LHD8	5' and 3' truncations in transcript evidence prevent annotation of the start and the end of the CDS. CDS 5' and 3' incomplete TSL:5
Nrg1-216	ENSMUST000000208931.1	407	135aa	Protein coding	-	A0A140LHQ6	5' and 3' truncations in transcript evidence prevent annotation of the start and the end of the CDS. CDS 5' and 3' incomplete TSL:5
Nrg1-214	ENSMUST000000208819.1	2322	287aa	Nonsense mediated decay	-	A0A140LHG5	TSL:5
Nrg1-209	ENSMUST000000208355.1	285	No protein	Processed transcript	-	-	TSL:5
Nrg1-207	ENSMUST000000208206.1	2086	No protein	Retained intron	-	-	TSL:NA
Nrg1-215	ENSMUST000000208820.1	1628	No protein	Retained intron	-	-	TSL:1
Nrg1-204	ENSMUST000000207584.1	1502	No protein	Retained intron	-	-	TSL:1
Nrg1-205	ENSMUST000000207678.1	1415	No protein	Retained intron	-	-	TSL:1

The strategy is based on the design of *Nrg1-201* transcript,The transcription is shown below



Genomic location distribution



Protein domain

ENSMUSP00000073...

Transmembrane heli...

MobiDB lite

Low complexity (Seg)

Conserved Domains

hmmpantther

Superfamily domains

SMART domains

Prints domain

Pfam domain

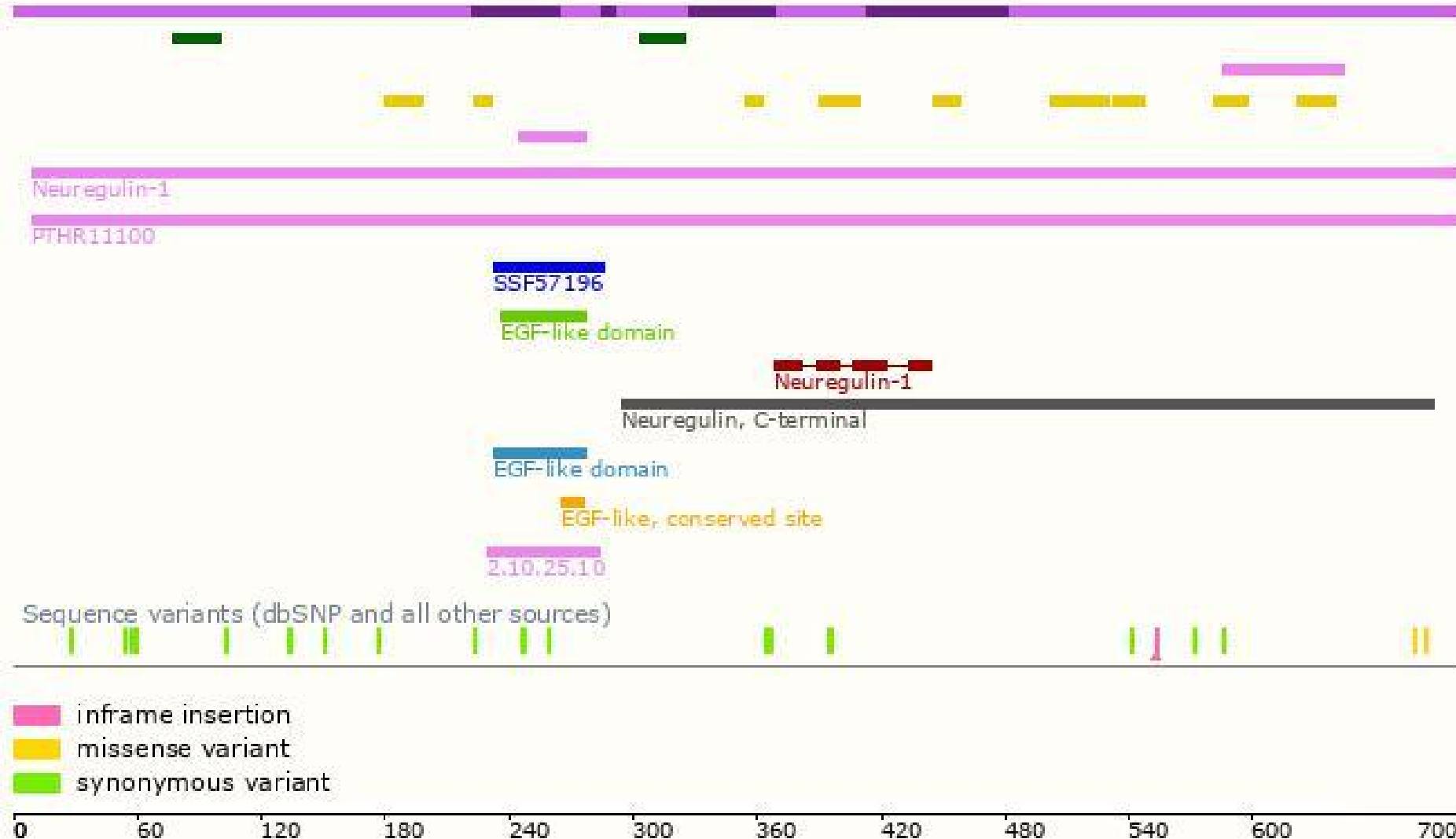
PROSITE profiles

PROSITE patterns

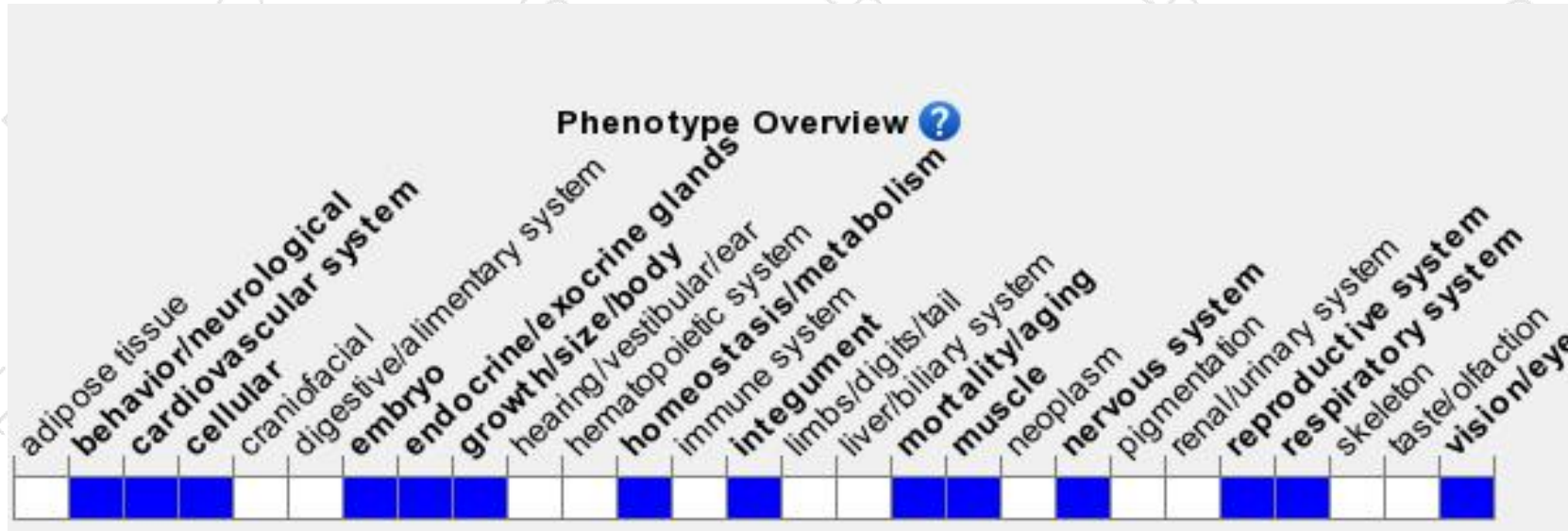
Gene3D

All sequence SNPs/i....

Variant Legend



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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