Nrg1 Cas9-KO Strategy

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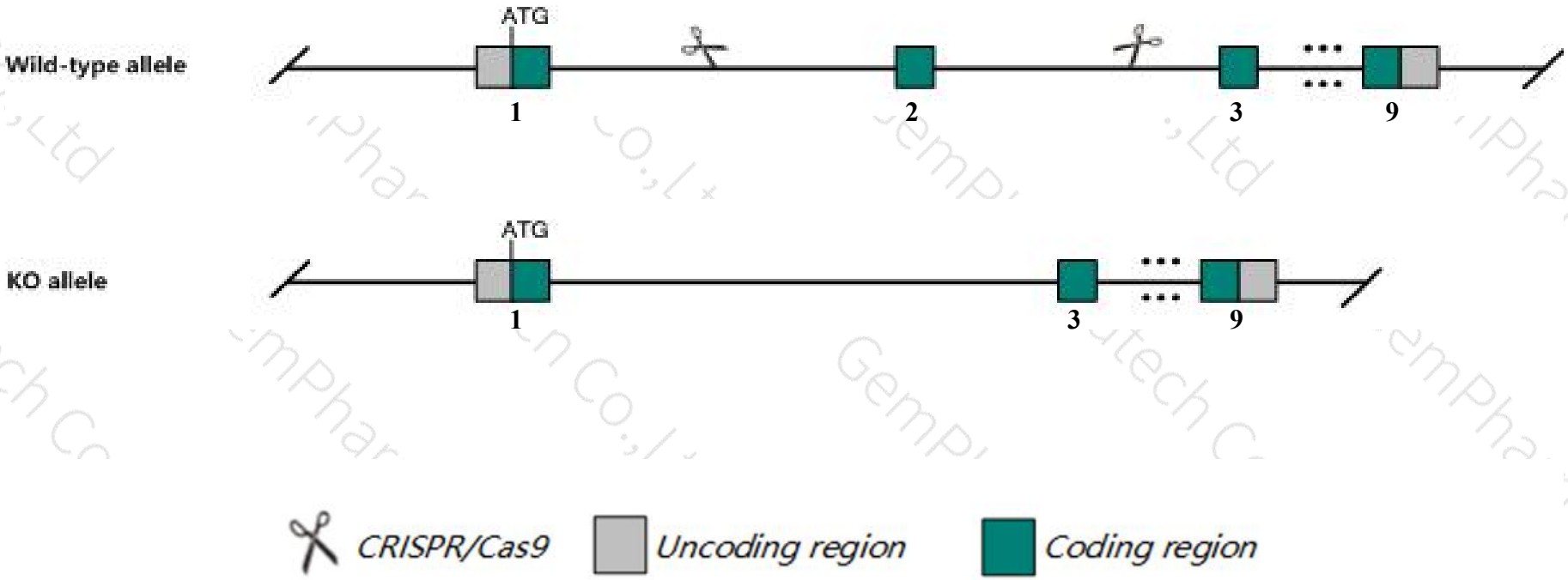
Project Overview

Project Name	***Nrg1***
Project type	**Cas9-KO**
Strain background	**C57BL/6JGpt**

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 v

Notice

➢ 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 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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Nrg1 neuregulin 1 [Mus musculus (house mouse)]

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

Summary

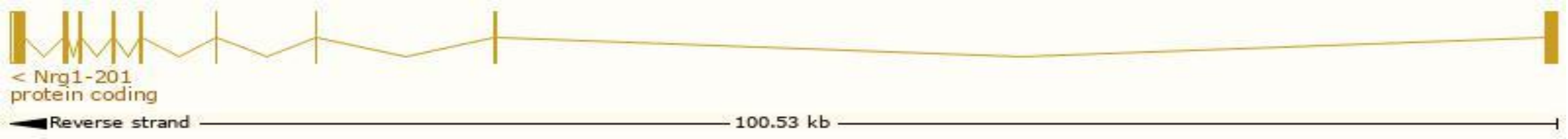
Official Symbol	Nrg1 provided by MGI
Official Full Name	neuregulin 1 provided byMGI
Primary source	MGI:MGI:96083
See related	Ensembl:ENSMUSG00000062991
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; 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 tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

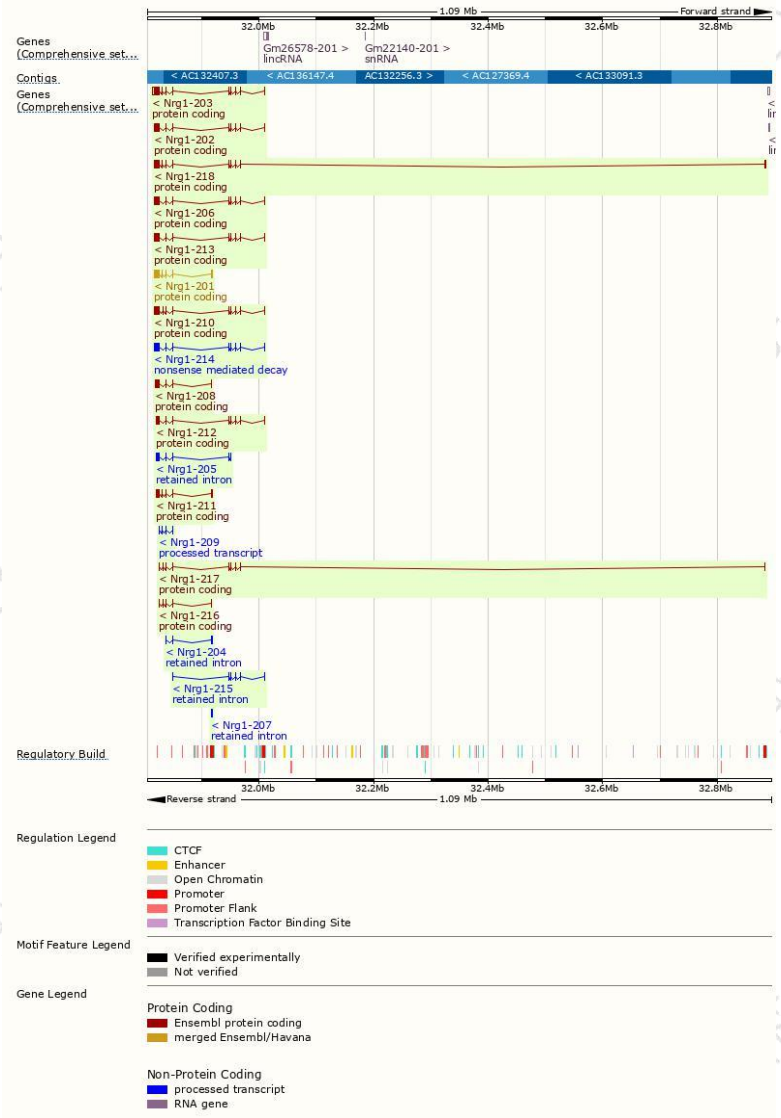
The gene has 18 transcripts,all transcripts are shown below:

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	ENSMUST00000207470.1	5415	645aa	Protein coding	-	Q6DR98	TSL:1 GENCODE basic APPRIS ALT2
Nrg1-202	ENSMUST00000207417.1	3138	637aa	Protein coding	-	A0A140LIP8	TSL:5 GENCODE basic APPRIS ALT2
Nrg1-218	ENSMUST00000209107.1	2972	652aa	Protein coding	-	A0A140LHZ9	TSL:5 GENCODE basic APPRIS ALT2
Nrg1-213	ENSMUST00000208617.1	2787	462aa	Protein coding	-	A0A140LIK5	TSL:5 GENCODE basic
Nrg1-206	ENSMUST00000208205.1	2645	640aa	Protein coding	-	A0A140LJC1	TSL:5 GENCODE basic APPRIS ALT2
Nrg1-210	ENSMUST00000208488.1	2403	663aa	Protein coding	-	A0A140LJ88	TSL:5 GENCODE basic
Nrg1-211	ENSMUST00000208497.1	2096	483aa	Protein coding	-	A0A140LIG9	TSL:1 GENCODE basic
Nrg1-212	ENSMUST00000208598.1	1778	423aa	Protein coding	-	A0A140LHN1	TSL:5 GENCODE basic
Nrg1-217	ENSMUST00000209022.1	1026	266aa	Protein coding	-	A0A140LIJ3	CDS 3' incomplete TSL:5
Nrg1-208	ENSMUST00000208335.1	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	ENSMUST00000208931.1	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	ENSMUST00000208819.1	2322	287aa	Nonsense mediated decay	-	A0A140LHG5	TSL:5
Nrg1-209	ENSMUST00000208355.1	285	No protein	Processed transcript	-	-	TSL:5
Nrg1-207	ENSMUST00000208206.1	2086	No protein	Retained intron	-	-	TSL:NA
Nrg1-215	ENSMUST00000208820.1	1628	No protein	Retained intron	-	-	TSL:1
Nrg1-204	ENSMUST00000207584.1	1502	No protein	Retained intron	-	-	TSL:1
Nrg1-205	ENSMUST00000207678.1	1415	No protein	Retained intron	-	-	TSL:1

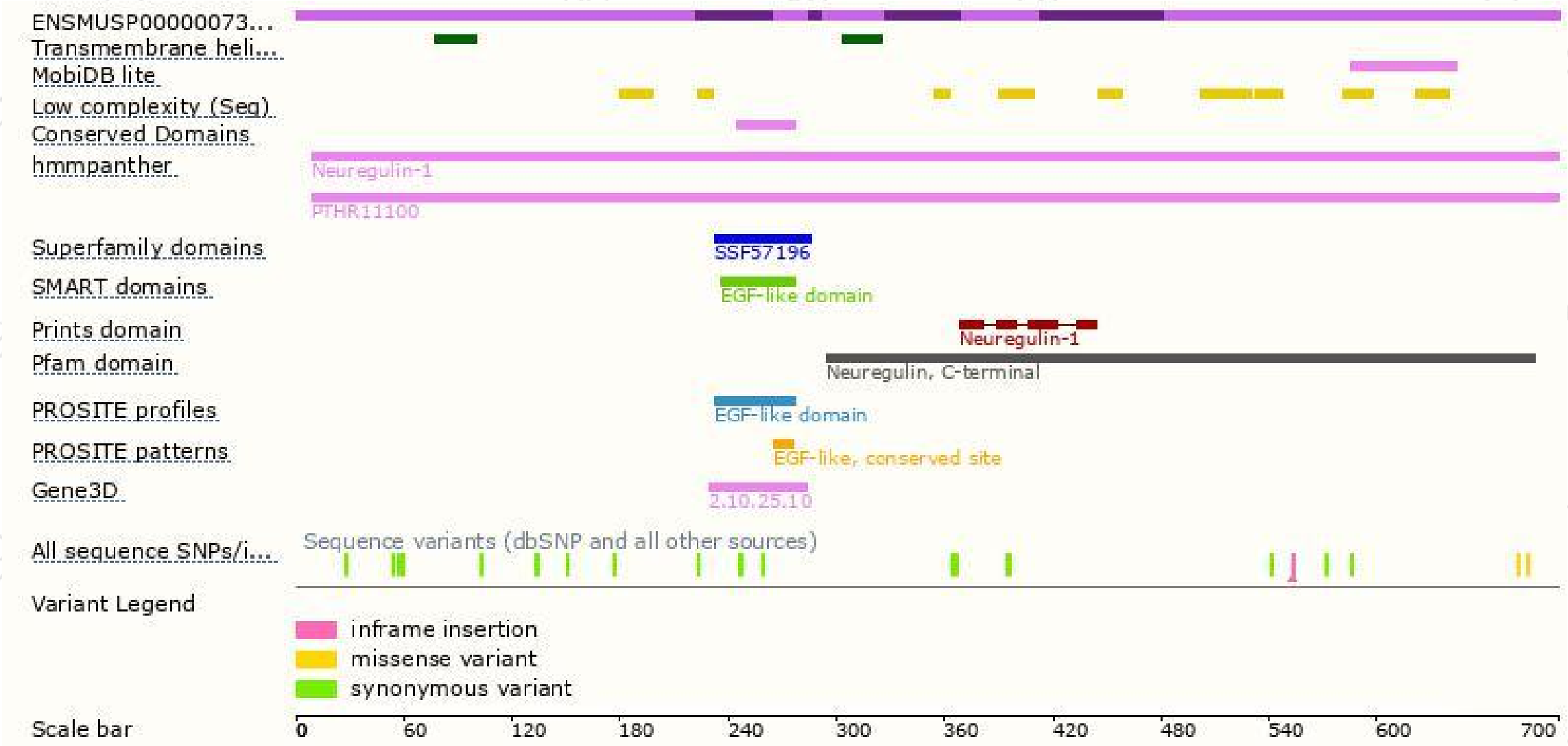
The strategy is based on the design of *Nrg1-201* transcript,The transcription is shown below



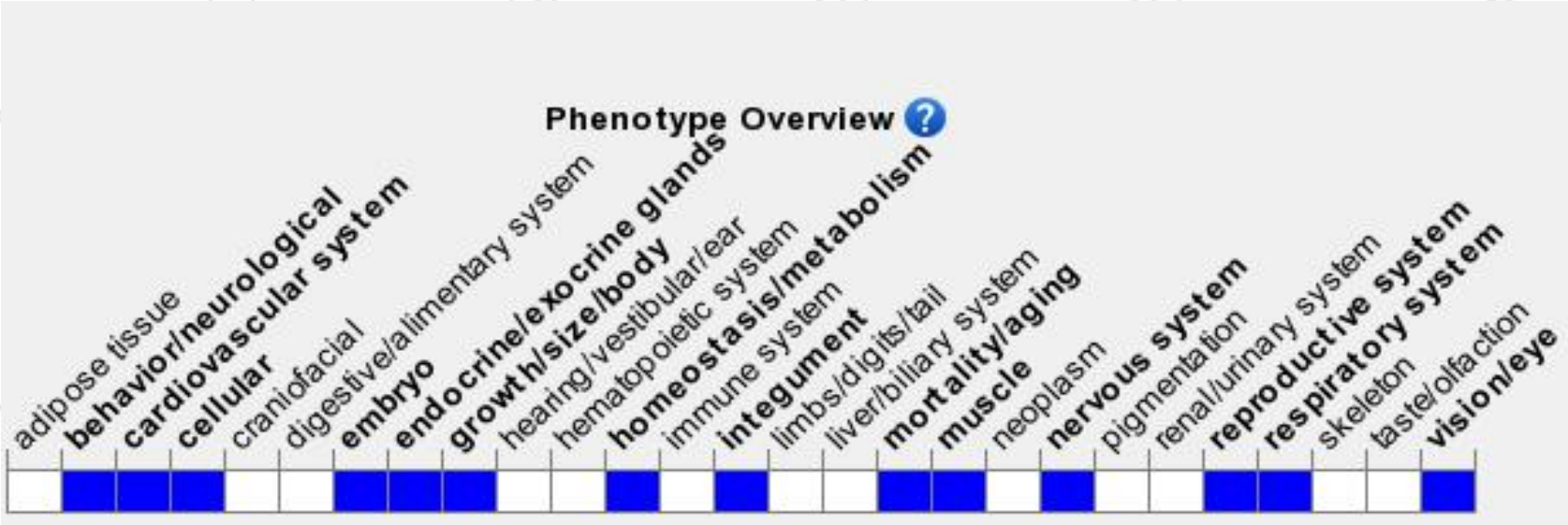
Genomic location distribution



Protein domain



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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