

# Lrp8 Cas9-KO Strategy

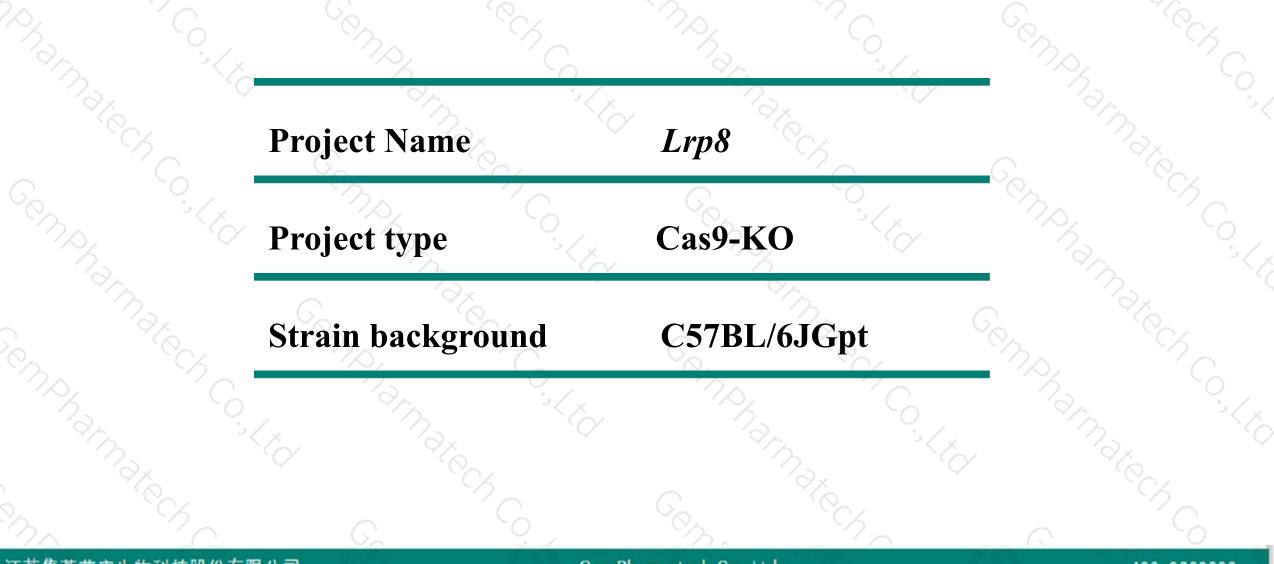
Designer: Reviewer:

**Design Date:** 

Daohua Xu Huimin Su 2019-11-14

# **Project Overview**





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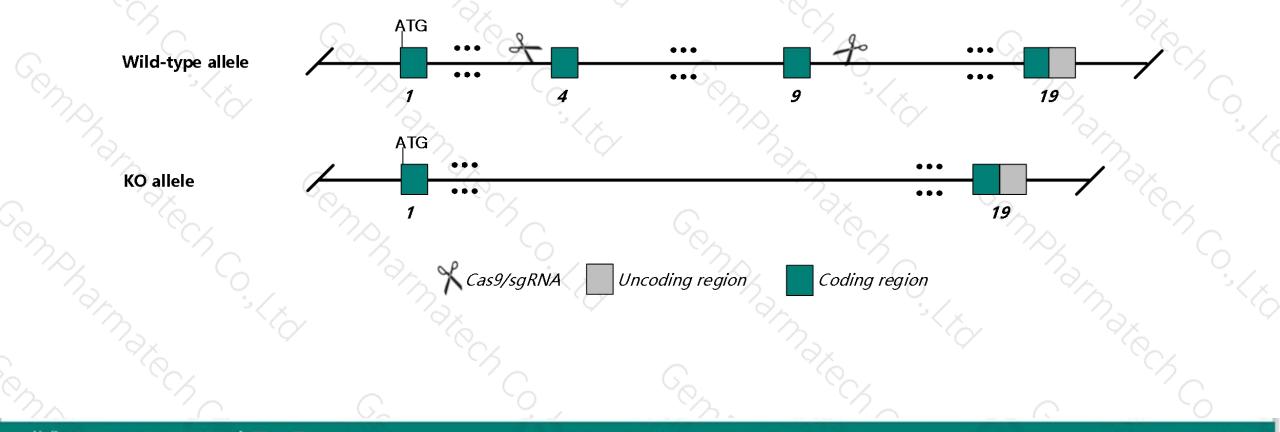
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## **Knockout strategy**



400-9660890

This model will use CRISPR/Cas9 technology to edit the *Lrp8* gene. The schematic diagram is as follows:



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- The Lrp8 gene has 23 transcripts. According to the structure of Lrp8 gene, exon4-exon9 of Lrp8-203 transcript is recommended as the knockout region. The region contains 799bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Lrp8* gene. The brief process is as follows:CRISPR/Cas9 system 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.



- According to the existing MGI data, Homozygotes for a targeted null mutation exhibit impaired granule cell migration, radial glial scaffold formation, contextual fear conditioning, and long-term potentiation. Mutant males have abnormal sperm and are sterile.
- The Lrp8 gene is located on the Chr4. 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 gene knockout on gene transcription, RNA splicing and protein translation cannot be predicted at existing technological level.

# **Gene information (NCBI)**



	Lrp8 low density lipoprotein receptor-related protein 8, apolipoprotein e receptor [Mus musculus (house mouse)]							
	Gene ID: 16975, updated	on 16-Mar-2019						
	Summary		(*)					
	Official Symbol	Lrp8 provided by MGI						
	Official Full Name	low density lipoprotein receptor-related protein 8, apolipoprotein e receptor provided by MGI						
	Primary source	MGI:MGI:1340044						
	See related	Ensembl:ENSMUSG0000028613						
	Gene type	protein coding						
	<b>RefSeq status</b>	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	4932703M08Rik, AA921429, Al848122, ApoER2, Lr8b						
	Expression	ion Biased expression in CNS E18 (RPKM 24.6), whole brain E14.5 (RPKM 23.2) and 14 other tissues See more						
	Orthologs	human all						

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# **Transcript information (Ensembl)**



#### The gene has 23 transcripts, all transcripts are shown below:

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Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Lrp8-202	ENSMUST00000106731.3	7391	<u>870aa</u>	Protein coding	CCDS51255	F6YZZ8	TSL:1 GENCODE basic
Lrp8-220	ENSMUST00000238584.1	4618	<u>828aa</u>	Protein coding			GENCODE basic
Lrp8-201	ENSMUST00000030356.9	4555	<u>955aa</u>	Protein coding	10	B1AXJ4	TSL:5 GENCODE basic
Lrp8-218	ENSMUST00000238569.1	3497	<u>996aa</u>	Protein coding	12	1025	GENCODE basic APPRIS P1
Lrp8-204	ENSMUST00000106733.9	3333	<u>896aa</u>	Protein coding	7	B1AXJ5	TSL:5 GENCODE basic
Lrp8-221	ENSMUST00000238651.1	2799	<u>726aa</u>	Protein coding			GENCODE basic
Lrp8-206	ENSMUST00000126573.7	2590	<u>694aa</u>	Protein coding	10	B1AXJ6	TSL:5 GENCODE basic
Lrp8-203	ENSMUST00000106732.9	2531	<u>832aa</u>	Protein coding	12	B1AXJ3	CDS 5' incomplete TSL:1
Lrp8-217	ENSMUST00000238421.1	2364	<u>787aa</u>	Protein coding		1.0	GENCODE basic
Lrp8-214	ENSMUST00000238255.1	1105	<u>189aa</u>	Protein coding	. ×		CDS 5' incomplete
Lrp8-223	ENSMUST00000238693.1	764	<u>124aa</u>	Protein coding	2	020	CDS 5' incomplete
Lrp8-207	ENSMUST00000135022.2	471	<u>157aa</u>	Protein coding	12	323	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
Lrp8-209	ENSMUST00000143601.7	3291	<u>996aa</u>	Nonsense mediated decay		<u>Q924X6</u>	TSL1
Lrp8-222	ENSMUST00000238658.1	1074	<u>135aa</u>	Nonsense mediated decay			CDS 5' incomplete
Lrp8-210	ENSMUST00000145832.1	2629	No protein	Retained intron	2	0.20	TSL1
Lrp8-213	ENSMUST00000238207.1	1434	No protein	Retained intron	<u>.</u>	3.25	
Lrp8-215	ENSMUST00000238304.1	822	No protein	Retained intron			
Lrp8-216	ENSMUST00000238405.1	737	No protein	Retained intron			
Lrp8-208	ENSMUST00000135591.1	557	No protein	Retained intron	-	040	TSL:5
Lrp8-219	ENSMUST00000238570.1	3532	No protein	IncRNA	<u> </u>	3.95	
Lrp8-205	ENSMUST00000123140.7	3129	No protein	IncRNA			TSL1
Lrp8-211	ENSMUST00000146552.8	2713	No protein	IncRNA		(100)	TSL:5
Lrp8-212	ENSMUST00000147319.7	797	No protein	IncRNA	10	(a)	TSL:5

The strategy is based on the design of Lrp8-203 transcript, The transcription is shown below

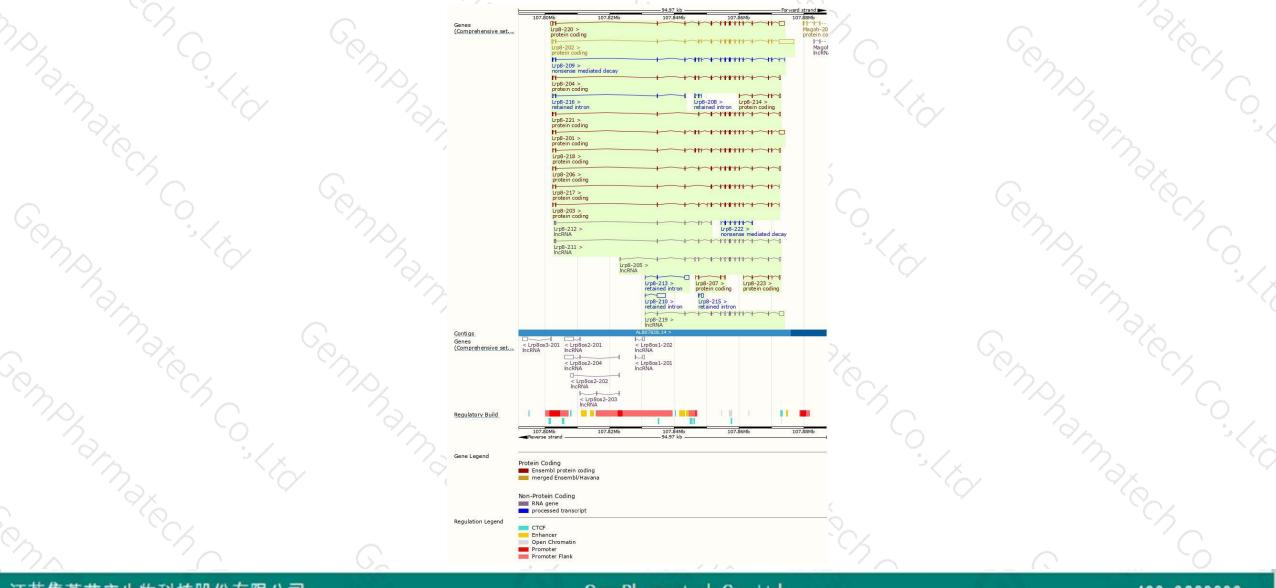


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### **Genomic location distribution**



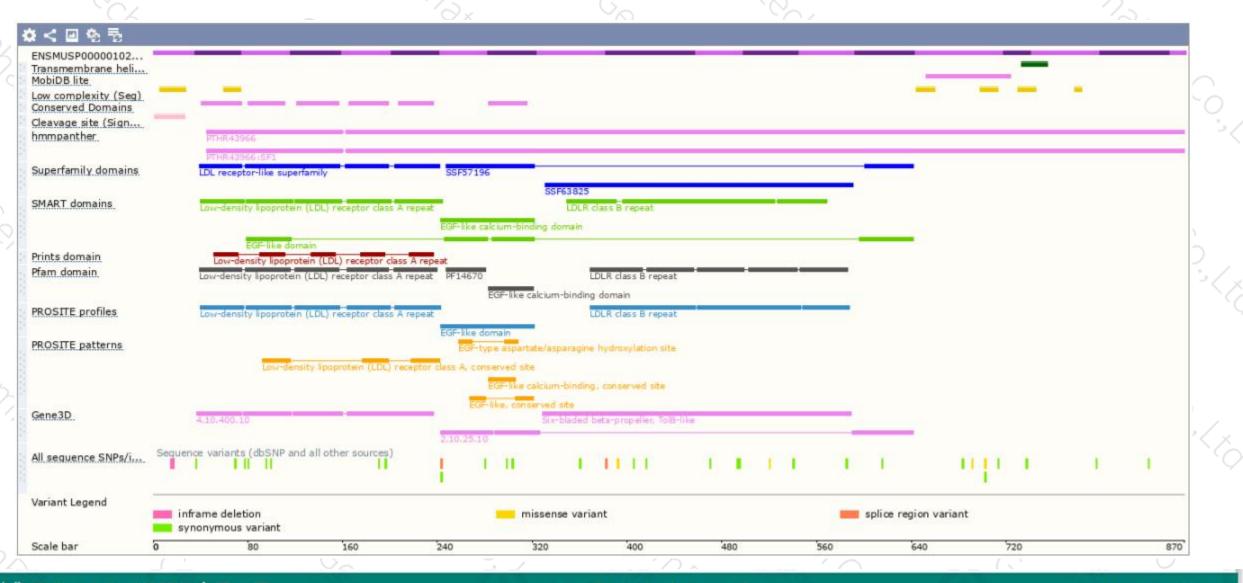


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### **Protein domain**



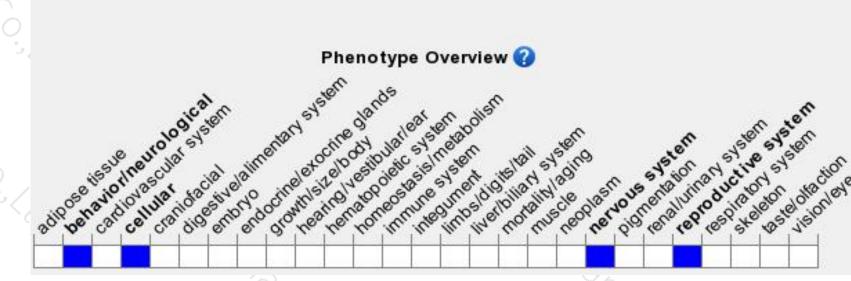


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### Mouse phenotype description(MGI)





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, Homozygotes for a targeted null mutation exhibit impaired granule cell migration, radial glial scaffold formation, contextual fear conditioning, and long-term potentiation. Mutant males have abnormal sperm and are sterile.



If you have any questions, you are welcome to inquire. Tel: 400-9660890



