

Lrp8 Cas9-KO Strategy

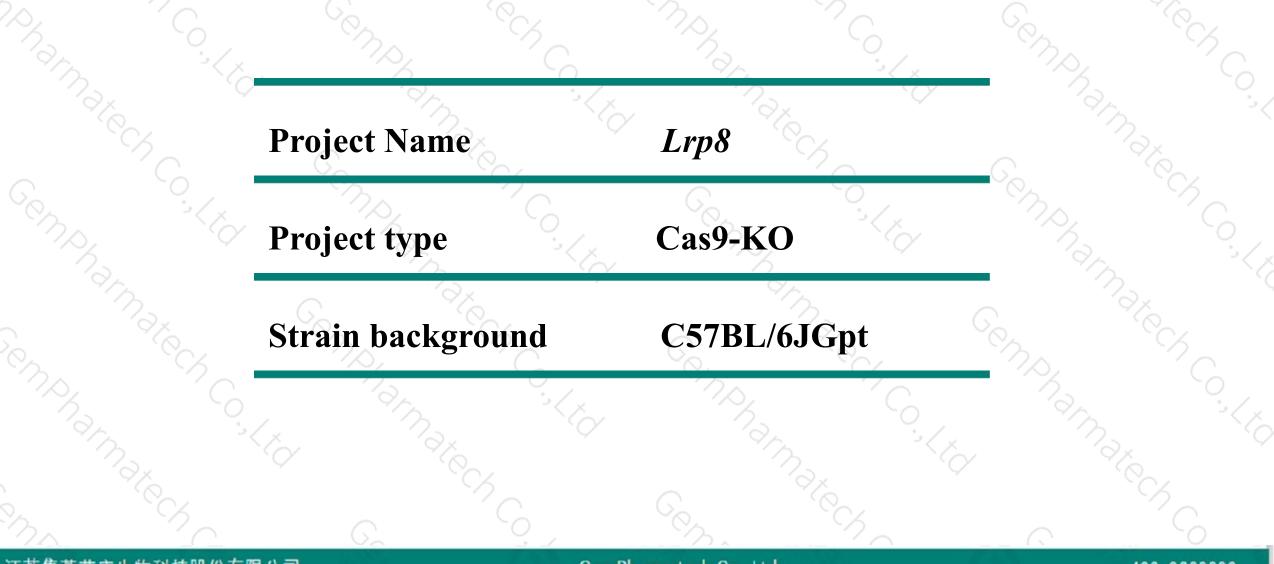
Designer: Reviewer:

Design Date:

Daohua Xu Huimin Su 2019-11-14

Project Overview





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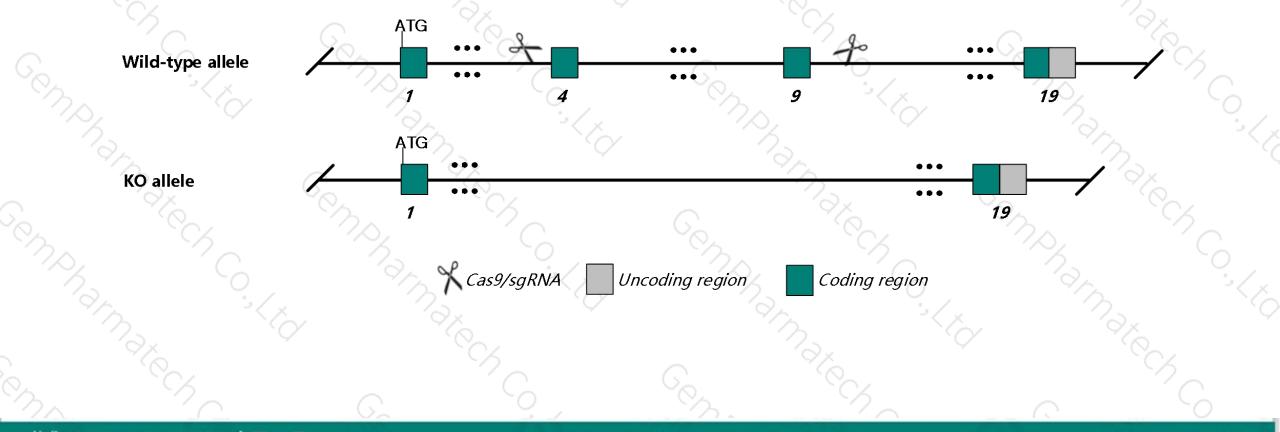
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Knockout strategy



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 | | | | | | |
| | 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 | 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:

| 5 / m | | | | | | · · · · · · · · · · · · · · · · · · · | |
|----------|----------------------|------|--------------|-------------------------|-----------|---------------------------------------|---|
| 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

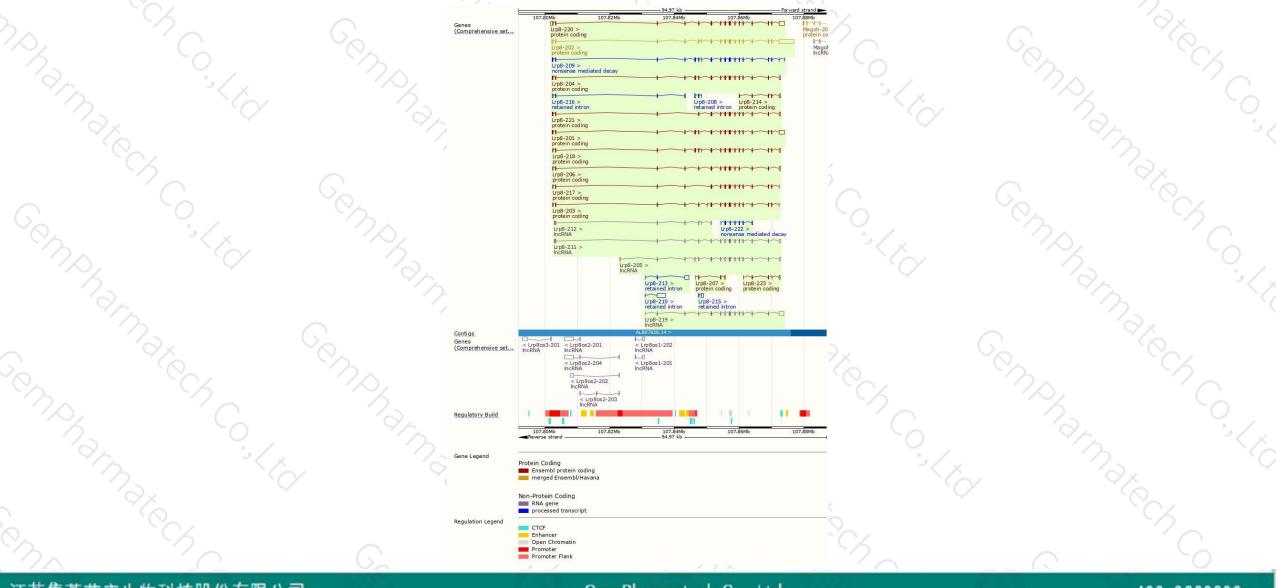


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Genomic location distribution



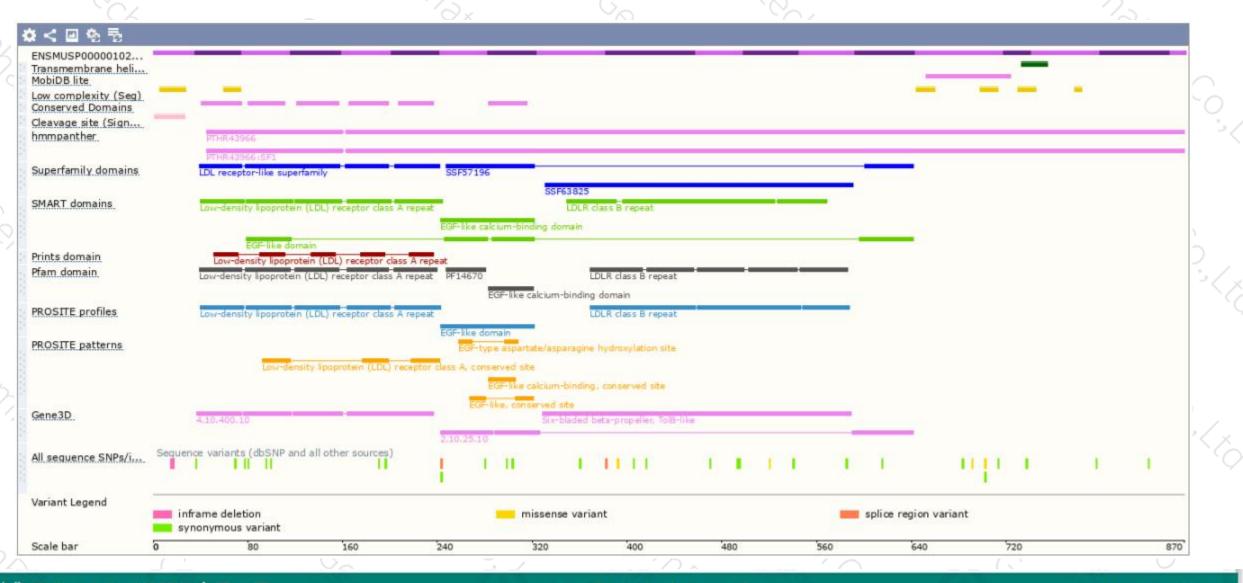


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Protein domain



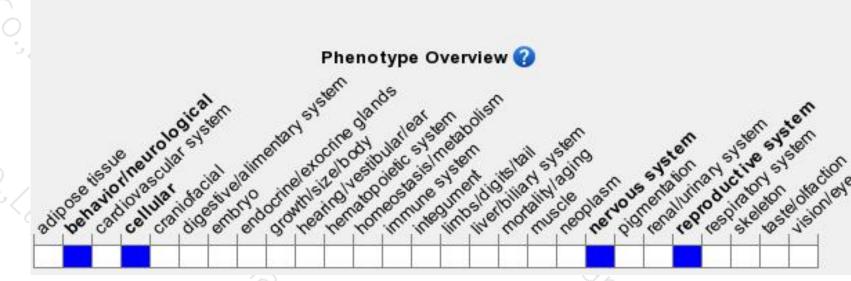


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Mouse phenotype description(MGI)





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



