Lrrk1 Cas9-CKO Strategy

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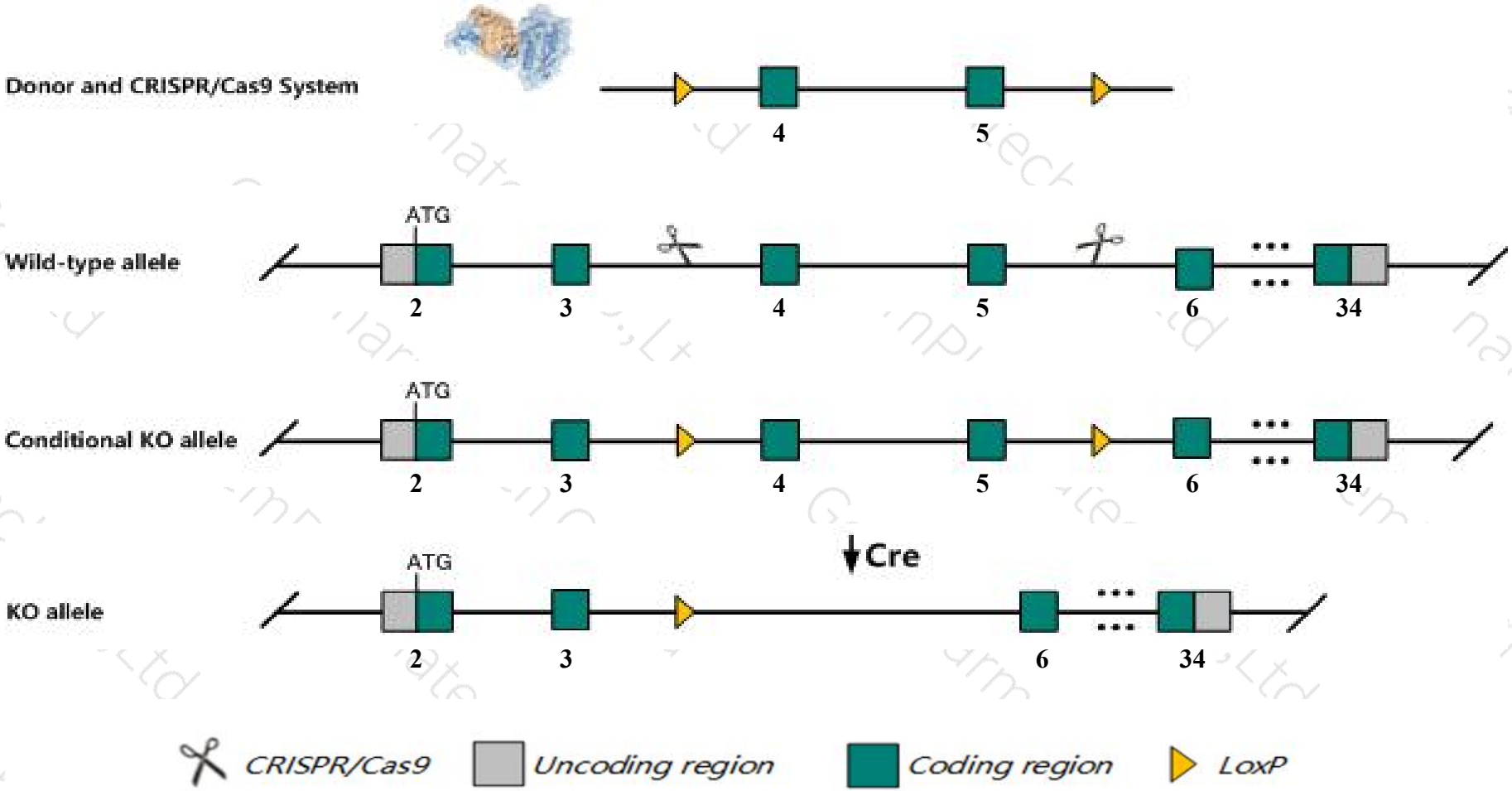
Project Overview

Project Name	***Lrrk1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Lrrk1* gene. The schematic diagram is as follows:



Technical routes

- The *Lrrk1* gene has 7 transcripts. According to the structure of *Lrrk1* gene, exon4-exon5 of *Lrrk1-201* (ENSMUST00000015277.13) transcript is recommended as the knockout region.The region contains 352bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Lrrk1* 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,Mice homozygous for a knock-out allele exhibit preweaning lethality.
Mice homozygous for another knock-out allele exhibit severe osteopetrosis.

➢ The *Lrrk1* gene is located on the Chr7. 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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Lrrk1 leucine-rich repeat kinase 1 [*Mus musculus* (house mouse)]

Gene ID: 233328, updated on 10-Oct-2019

Summary

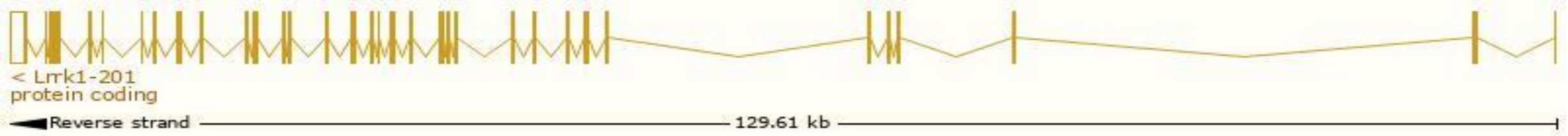
Official Symbol	Lrrk1 provided by MGI
Official Full Name	leucine-rich repeat kinase 1 provided by MGI
Primary source	MGI:MGI:2142227
See related	Ensembl:ENSMUSG00000015133
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	AW319595; mKIAA1790; C230002E15Rik; D130026O16Rik
Expression	Broad expression in lung adult (RPKM 12.7), ovary adult (RPKM 8.3) and 23 other tissues See more
Orthologs	human all

Transcript information（Ensembl）

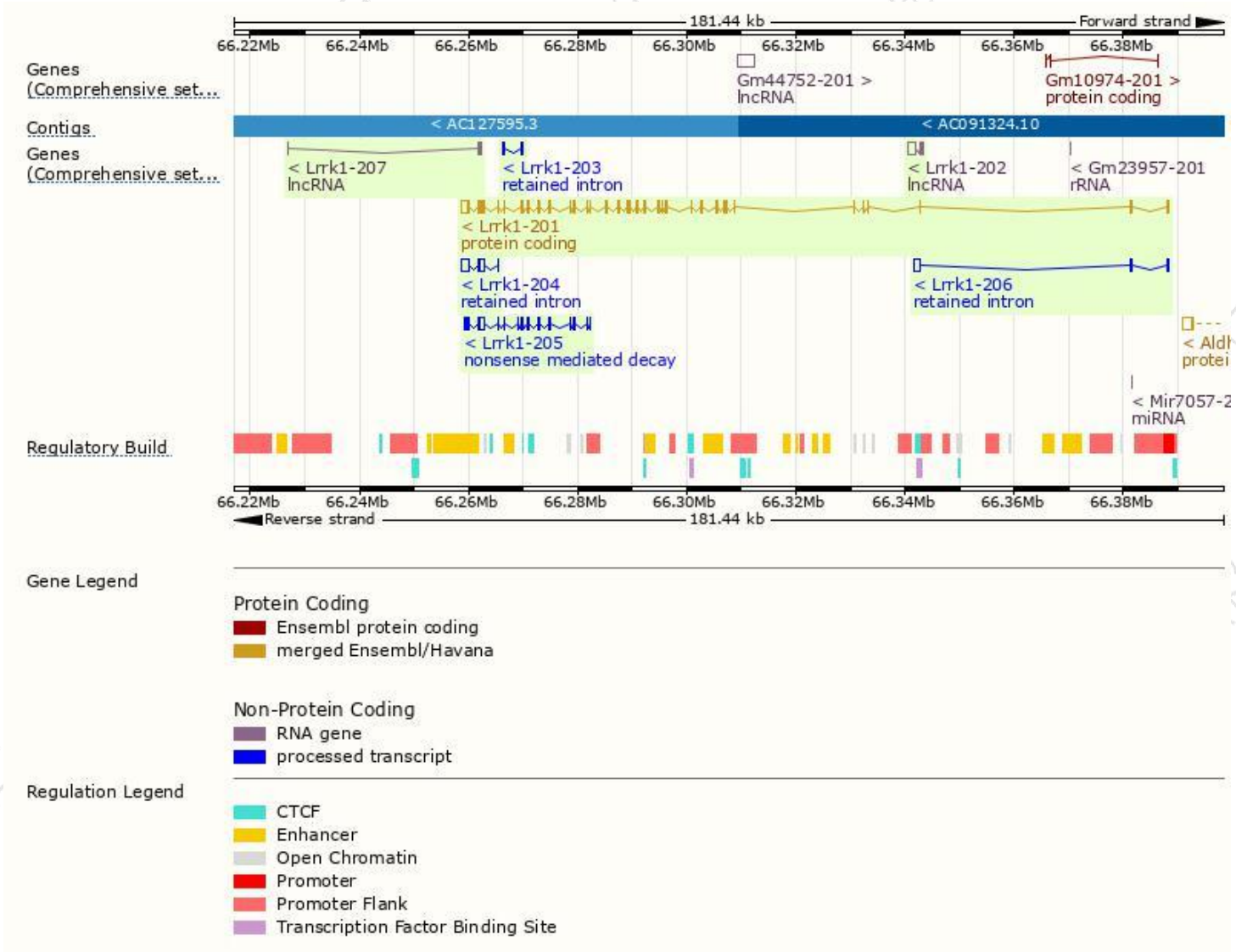
The gene has 7 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Lrrk1-201	ENSMUST00000015277.13	7465	2014aa	Protein coding	CCDS21344	Q3UHC2	TSL:1 GENCODE basic APPRIS P1
Lrrk1-205	ENSMUST00000145954.1	3374	508aa	Nonsense mediated decay	-	F6YIW9	CDS 5' incomplete TSL:1
Lrrk1-204	ENSMUST00000137181.7	2442	No protein	Retained intron	-	-	TSL:1
Lrrk1-206	ENSMUST00000154893.1	1559	No protein	Retained intron	-	-	TSL:1
Lrrk1-203	ENSMUST00000131239.1	482	No protein	Retained intron	-	-	TSL:2
Lrrk1-202	ENSMUST00000130438.2	1744	No protein	lncRNA	-	-	TSL:1
Lrrk1-207	ENSMUST00000167705.7	557	No protein	lncRNA	-	-	TSL:3

The strategy is based on the design of *Lrrk1-201* transcript,The transcription is shown below

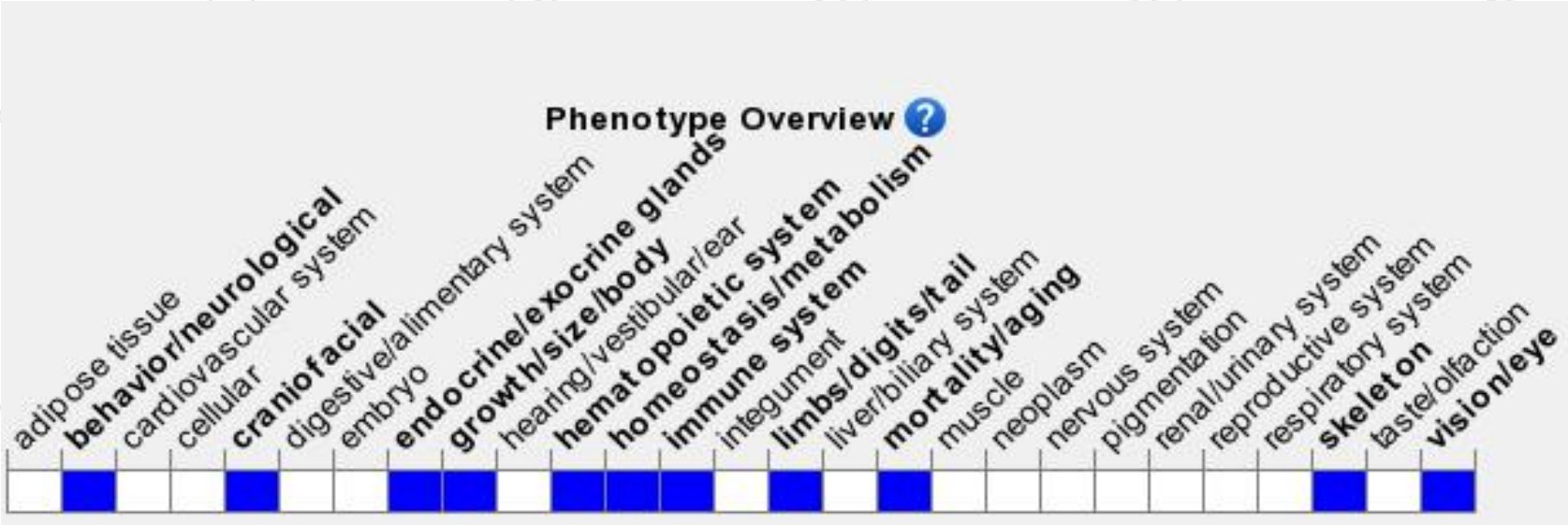


Genomic location distribution



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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