Fkbp1a Cas9-KO Strategy

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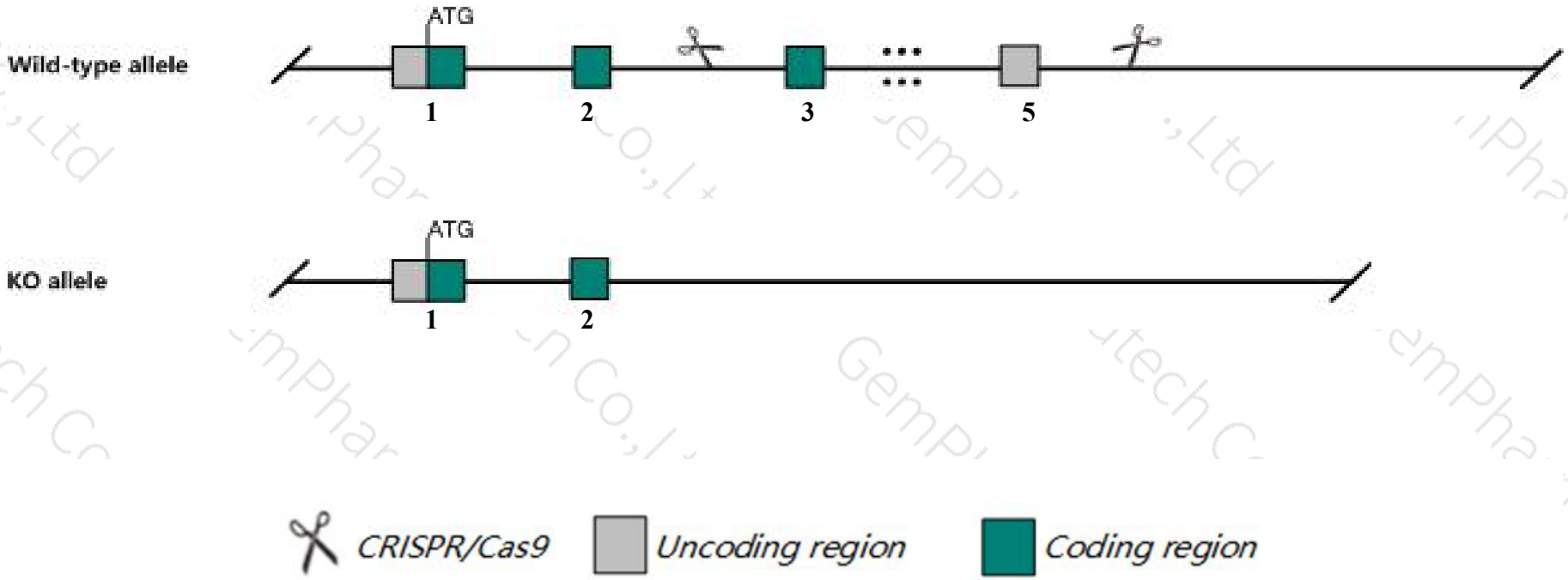
Project Overview

Project Name	***Fkbp1a***
Project type	**Cas9-KO**
Strain background	**C57BL/6JGpt**

Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Fkbp1a* gene. The schematic diagram is as follows:



Technical routes

➢ The *Fkbp1a* gene has 10 transcripts. According to the structure of *Fkbp1a* gene, exon3-exon5 of *Fkbp1a-201* (ENSMUST00000044011.11) transcript is recommended as the knockout region.The region contains 242bp coding sequence. Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Fkbp1a* gene. The brief process is as follows: CRISPR/Cas9 syster

Notice

- According to the existing MGI data,Mice homozygous for a null allele display embryonic and neonatal lethality and dilated cardiomyopathy associated with ventricular septal defects, myocardial noncompaction, a thin ventricular wall, hypertrophic trabeculae, and liver hemorrhage and necrosis; about 9% show neural tube closure defects.

- The *Fkbp1a* gene is located on the Chr2. 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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Fkbp1a FK506 binding protein 1a [Mus musculus (house mouse)]

Gene ID: 14225, updated on 28-Mar-2019

Summary

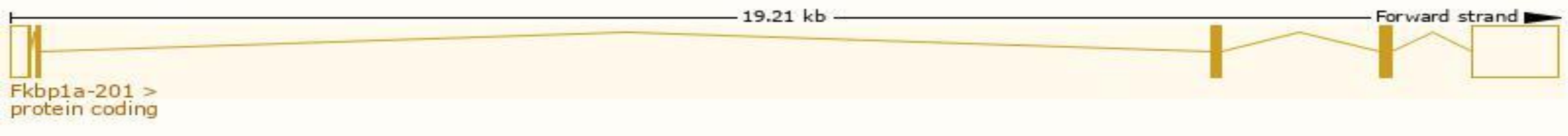
Official Symbol	Fkbp1a provided by MGI
Official Full Name	FK506 binding protein 1a provided byMGI
Primary source	MGI:MGI:95541
See related	Ensembl:ENSMUSG00000032966
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	FKBP12, Fkbp, Fkbp1
Summary	This gene is a member of the immunophilin family. The encoded protein is a cis-trans prolyl isomerase that binds the immunosuppressants FK506 and rapamycin, and is associated with immunoregulation, protein folding, receptor signaling, protein trafficking and T-cell activation. It may modulate the calcium release activity of the ryanodine receptor Ryr1. It also interacts with the type I TGF-beta receptor. Disruption of this gene in mouse causes severe ventricular defects. Pseudogenes of this gene have been defined on chromosomes 4, 10, 14, and 16. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Sep 2014]
Expression	Ubiquitous expression in cortex adult (RPKM 90.0), frontal lobe adult (RPKM 82.4) and 28 other tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

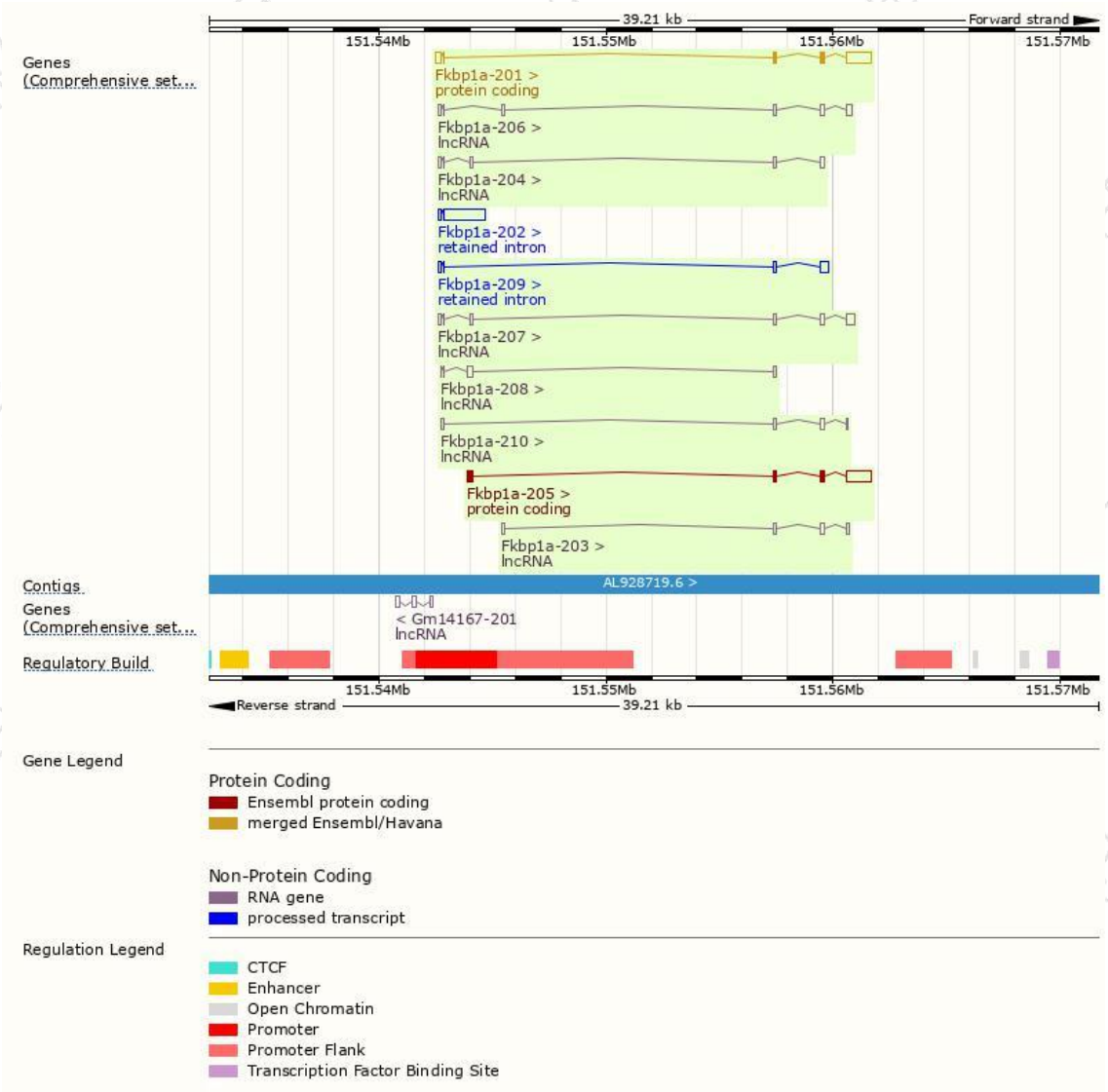
The gene has 10 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Fkbp1a-201	ENSMUST00000044011.11	1658	108aa	Protein coding	CCDS16869	P26883	TSL:1 GENCODE basic APPRIS P1
Fkbp1a-205	ENSMUST00000142271.1	1588	161aa	Protein coding	-	F6X9I3	CDS 5' incomplete TSL:1
Fkbp1a-202	ENSMUST00000126670.7	2011	No protein	Retained intron	-	-	TSL:2
Fkbp1a-209	ENSMUST00000148295.7	662	No protein	Retained intron	-	-	TSL:1
Fkbp1a-207	ENSMUST00000143230.7	894	No protein	lncRNA	-	-	TSL:3
Fkbp1a-206	ENSMUST00000142985.7	783	No protein	lncRNA	-	-	TSL:5
Fkbp1a-204	ENSMUST00000137597.7	603	No protein	lncRNA	-	-	TSL:3
Fkbp1a-203	ENSMUST00000132614.1	475	No protein	lncRNA	-	-	TSL:2
Fkbp1a-210	ENSMUST00000148978.7	438	No protein	lncRNA	-	-	TSL:2
Fkbp1a-208	ENSMUST00000144171.1	422	No protein	lncRNA	-	-	TSL:3

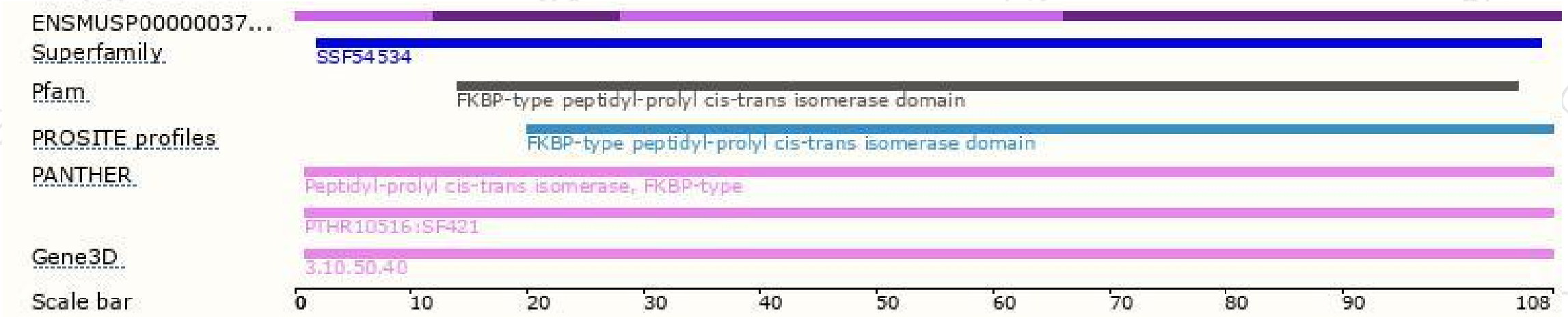
The strategy is based on the design of *Fkbp1a-201* transcript,The transcription is shown below



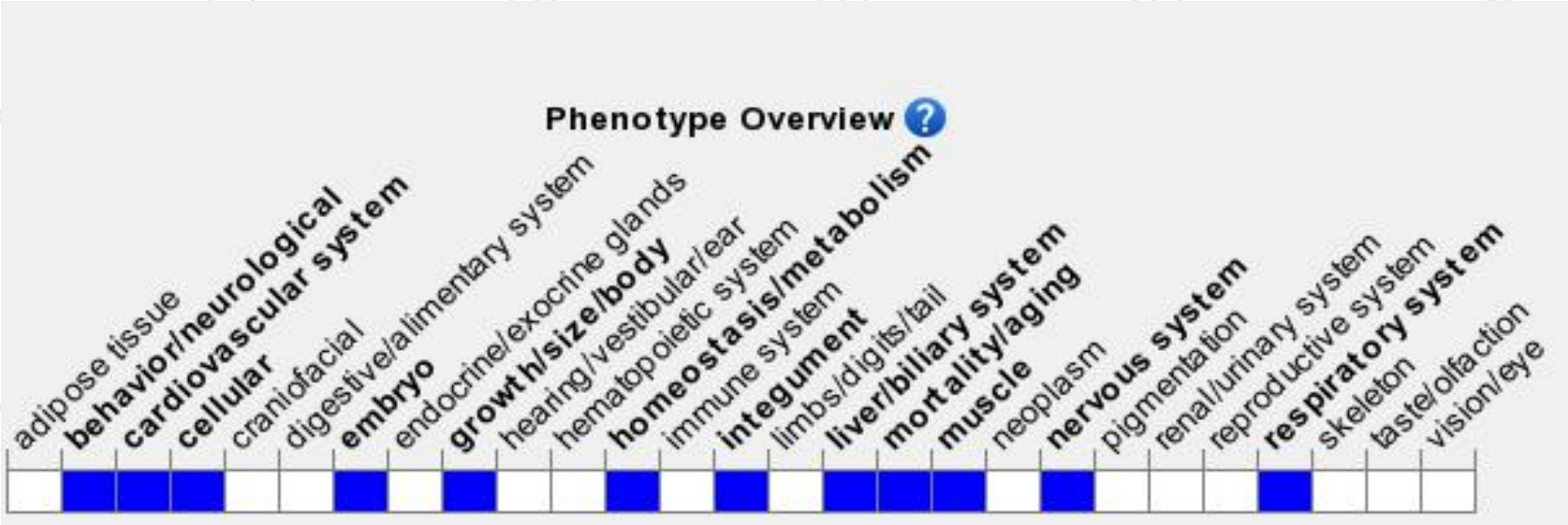
Genomic location distribution



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/).

According to the existing MGI data,Mice homozygous for a null allele display embryonic and neonatal lethality and dilated cardiomyopathy associated with ventricular septal defects, myocardial noncompaction, a thin ventricular wall, hypertrophic trabeculae, and liver hemorrhage and necrosis; about 9% show neural tube closure defects.

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If you have any questions, you are welcome to inquire.

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