Ldlr-KO Strategy

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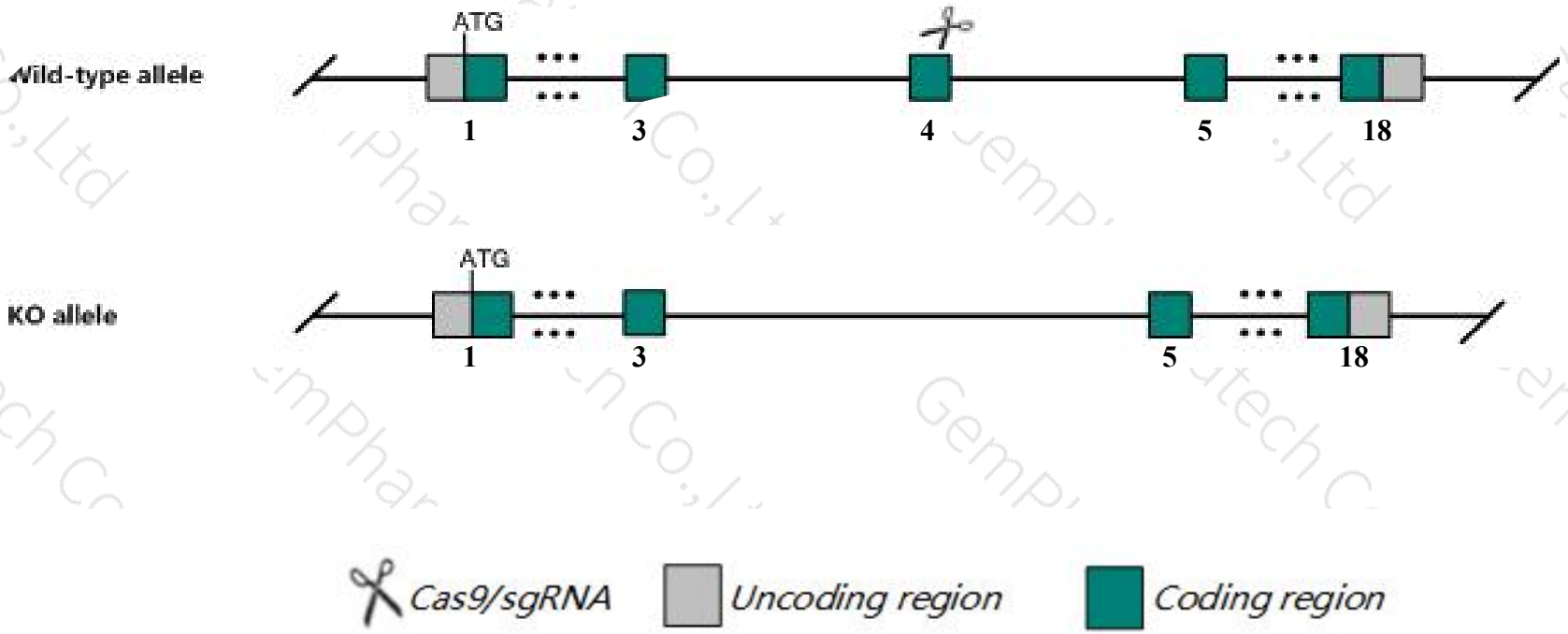
Project Overview

Project Name	***Ldlr***
Project type	**KO**
Strain background	**C57BL/6J**

Knockout strategy

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



Technical routes

➢ The *Ldlr* gene has 7 transcripts. According to the structure of *Ldlr* gene, a part of exon4 of *Ldlr-201* (ENSMUST00000034713.8) transcript is recommended as the knockout region.The region contains 82bp coding sequence. Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Ldlr* gene. The brief process is as follows: sgRNA was transcribed in vitro.Cas9 and sgRNA were microinjected into the fertilized eggs of C57BL/6J 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/6J mice.

Notice

➢ According to the existing MGI data,Homozygous targeted mutants exhibit 2X higher total plasma cholesterol and 7-9X higher IDL and LDL levels on a normal diet compared to controls. On a high cholesterol diet, mutant effects dramatically increase and mice develop xanthomatosis and atherosclerosis.

➢ The *Ldlr* gene is located on the Chr9. 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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Ldlr low density lipoprotein receptor [Mus musculus (house mouse)]

Gene ID: 16835, updated on 19-Mar-2019

Summary

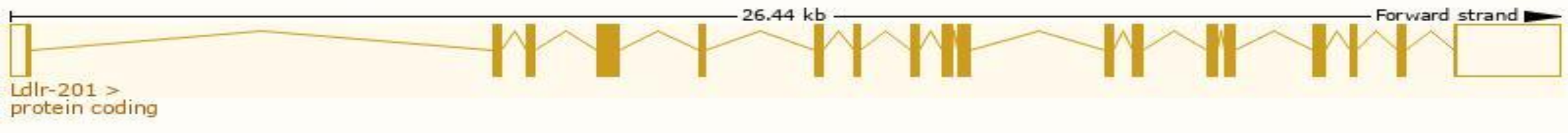
Official Symbol	Ldlr provided by MGI
Official Full Name	low density lipoprotein receptor provided by MGI
Primary source	MGI:MGI:96765
See related	Ensembl:ENSMUSG00000032193
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	Hlb301
Expression	Ubiquitous expression in colon adult (RPKM 56.3), adrenal adult (RPKM 52.3) and 27 other tissues See more
Orthologs	human all

Transcript information（Ensembl）

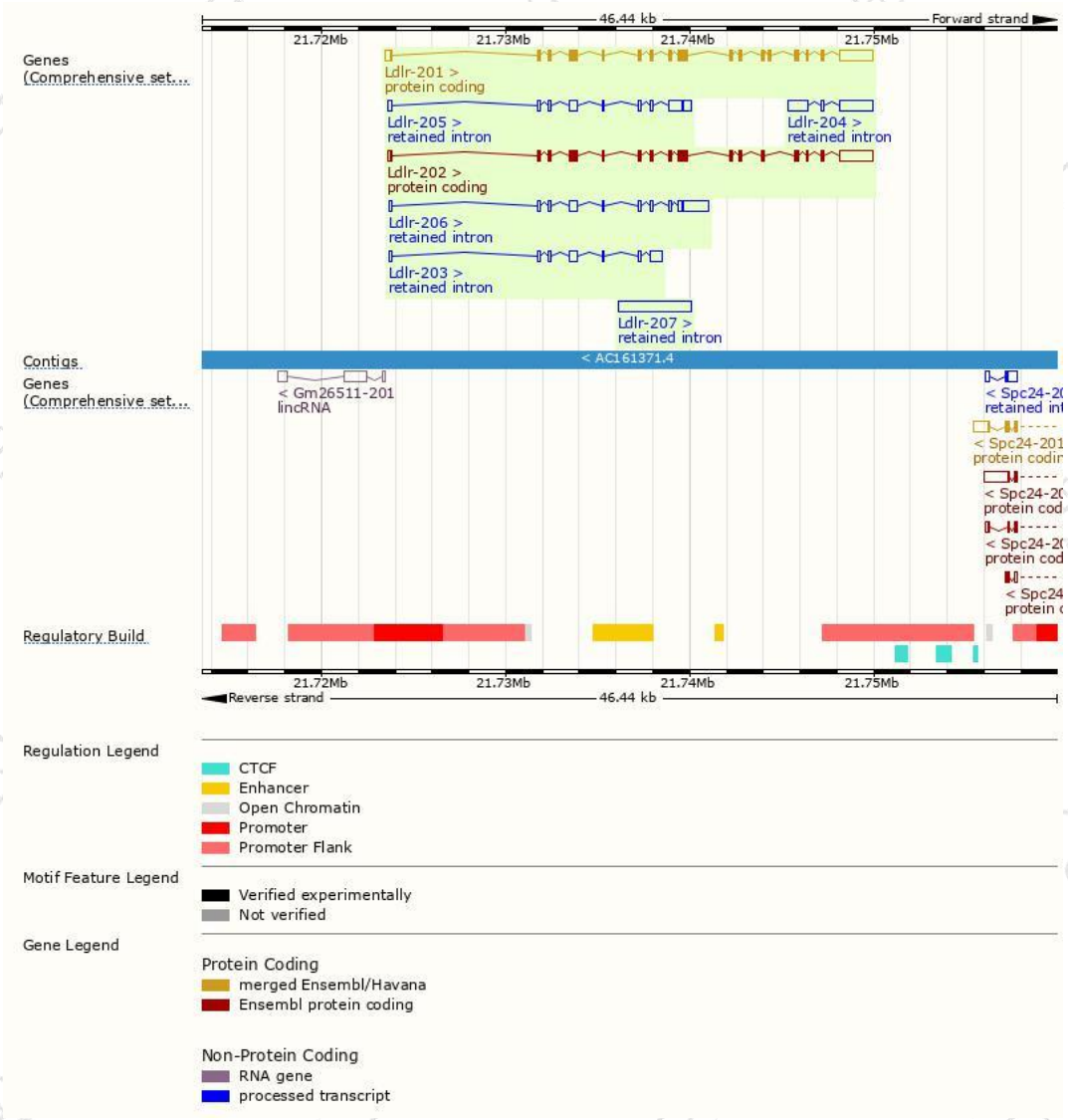
The gene has 7 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Ldlr-201	ENSMUST00000034713.8	4627	862aa	Protein coding	CCDS22910	P35951	TSL:1 GENCODE basic APPRIS P2
Ldlr-202	ENSMUST00000213114.1	4318	810aa	Protein coding	-	A0A1L1SRE8	TSL:1 GENCODE basic APPRIS ALT2
Ldlr-207	ENSMUST00000217613.1	3980	No protein	Retained intron	-	-	TSL:NA
Ldlr-204	ENSMUST00000214549.1	3049	No protein	Retained intron	-	-	TSL:1
Ldlr-206	ENSMUST00000217111.1	2854	No protein	Retained intron	-	-	TSL:1
Ldlr-205	ENSMUST00000215917.1	2383	No protein	Retained intron	-	-	TSL:1
Ldlr-203	ENSMUST00000214359.1	1739	No protein	Retained intron	-	-	TSL:1

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

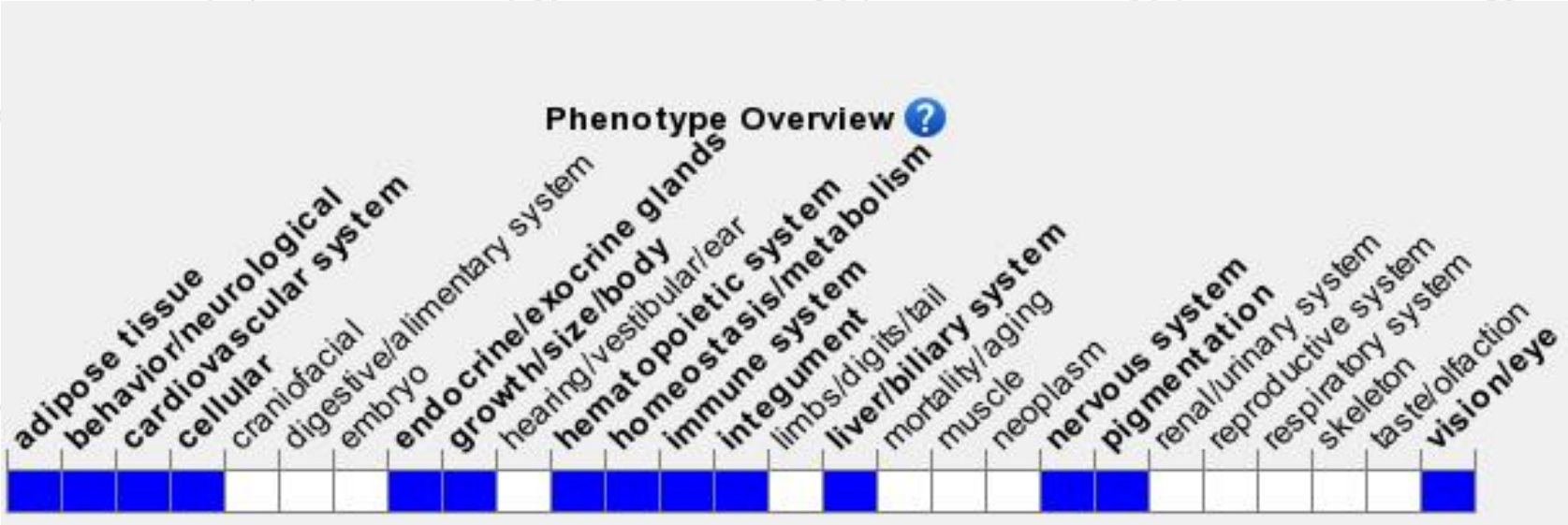


Genomic location distribution



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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