Lta4h Cas9-CKO Strategy

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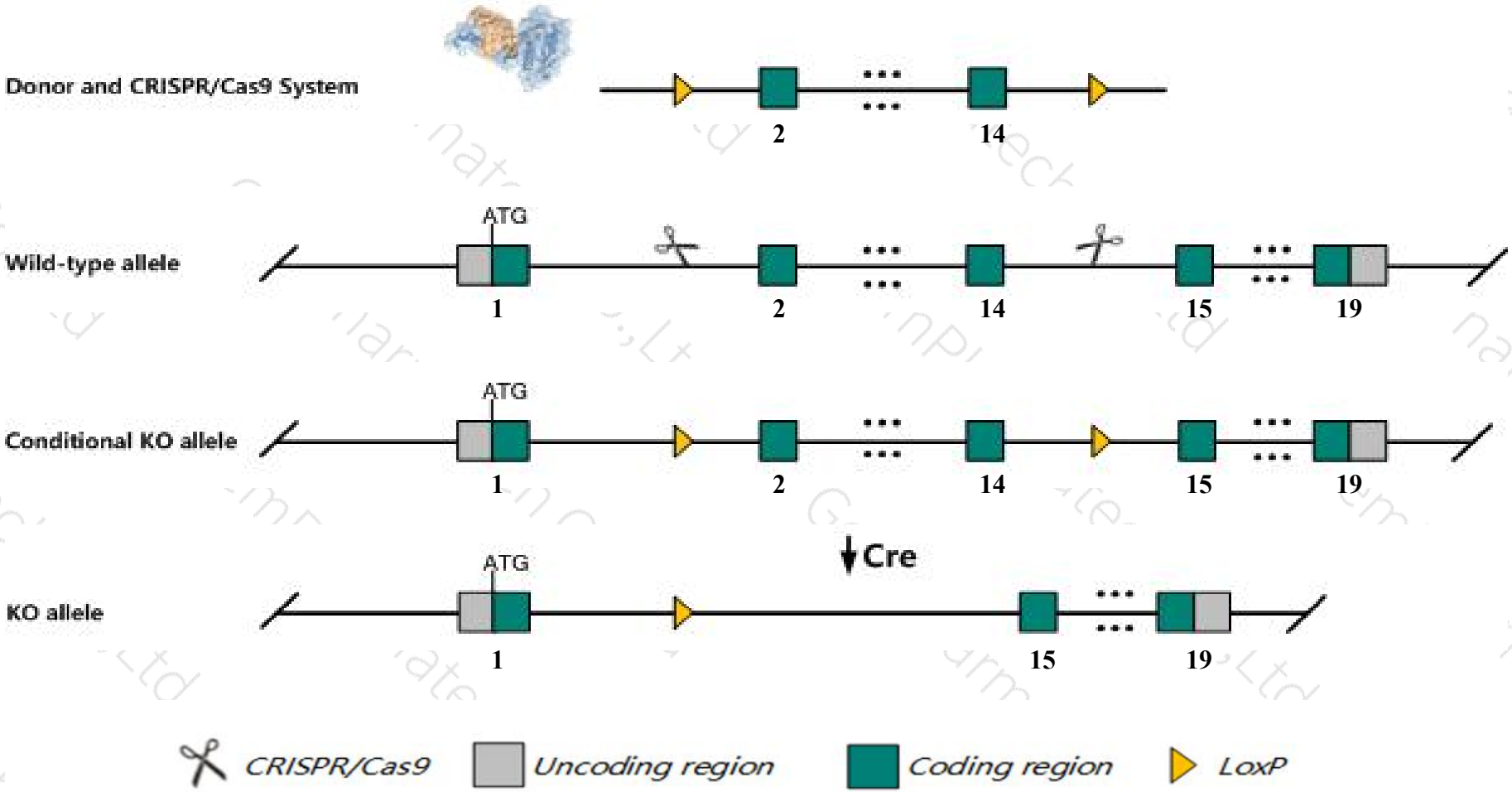
Project Overview

Project Name	***Lta4h***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Lta4h* gene. The schematic diagram is as follows:



Technical routes

- The *Lta4h* gene has 8 transcripts. According to the structure of *Lta4h* gene, exon2-exon14 of *Lta4h-201* (ENSMUST00000016033.8) transcript is recommended as the knockout region.The region contains 1220bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Lta4h* 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 disruptions in this gene have grossly normal phenotypes. Inflammatory reactions are reduced as are some other immunological responses.

- Transcript *Lta4h*-208 may not be affected.

- The *Lta4h* gene is located on the Chr10. 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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Lta4h leukotriene A4 hydrolase [Mus musculus (house mouse)]

Gene ID: 16993, updated on 19-Mar-2019

Summary

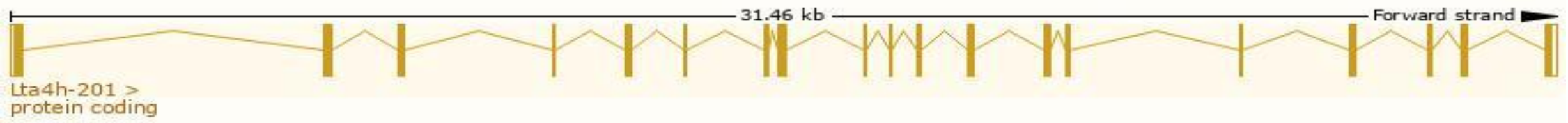
Official Symbol	Lta4h provided by MGI
Official Full Name	leukotriene A4 hydrolase provided byMGI
Primary source	MGI:MGI:96836
See related	Ensembl:ENSMUSG00000015889
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Summary	The protein encoded by this gene is an enzyme that contains both hydrolase and aminopeptidase activities. The hydrolase activity is used in the final step of the biosynthesis of leukotriene B4, a proinflammatory mediator. The aminopeptidase activity has been shown to degrade proline-glycine-proline (PGP), a neutrophil chemoattractant and biomarker for chronic obstructive pulmonary disease (COPD). Two transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Sep 2015]
Expression	Ubiquitous expression in large intestine adult (RPKM 63.2), duodenum adult (RPKM 45.9) and 28 other tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

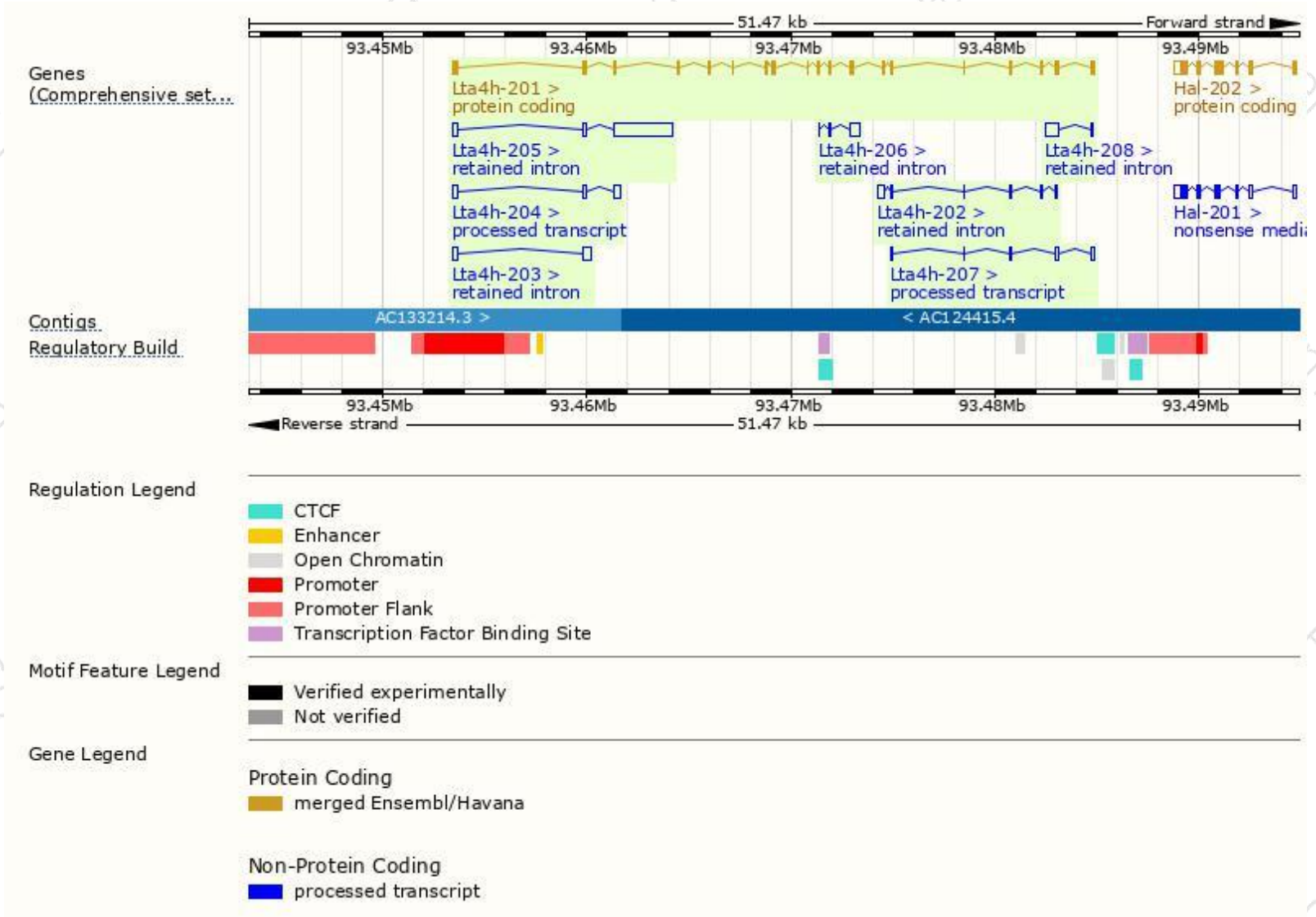
The gene has 8 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Lta4h-201	ENSMUST00000016033.8	2029	611aa	Protein coding	CCDS24125	P24527	TSL:1 GENCODE basic APPRIS P1
Lta4h-204	ENSMUST00000215419.1	687	No protein	Processed transcript	-	-	TSL:1
Lta4h-207	ENSMUST00000216931.1	540	No protein	Processed transcript	-	-	TSL:2
Lta4h-205	ENSMUST00000216146.1	3225	No protein	Retained intron	-	-	TSL:1
Lta4h-208	ENSMUST00000217556.1	752	No protein	Retained intron	-	-	TSL:2
Lta4h-202	ENSMUST00000214527.1	690	No protein	Retained intron	-	-	TSL:3
Lta4h-203	ENSMUST00000215224.1	629	No protein	Retained intron	-	-	TSL:2
Lta4h-206	ENSMUST00000216174.1	585	No protein	Retained intron	-	-	TSL:1

The strategy is based on the design of *Lta4h-201* transcript,The transcription is shown below

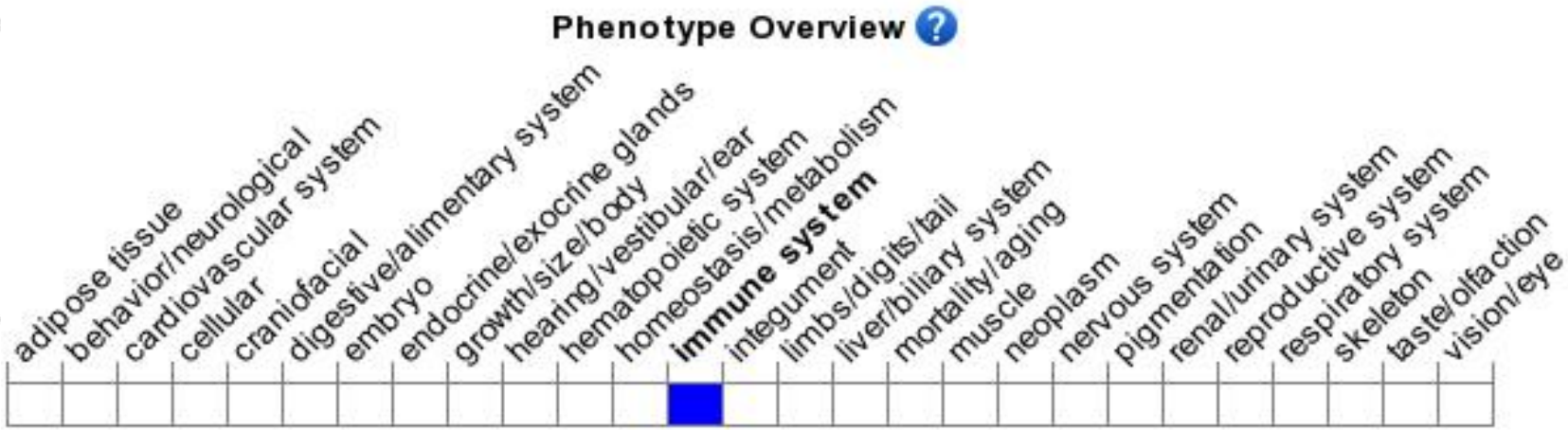


Genomic location distribution



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 disruptions in this gene have grossly normal phenotypes. Inflammatory reactions are reduced as are some other immunological responses.

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

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