GemPharmatech™

Apoc1 Cas9-CKO Strategy

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Overview

Target Gene Name

- Apoc1

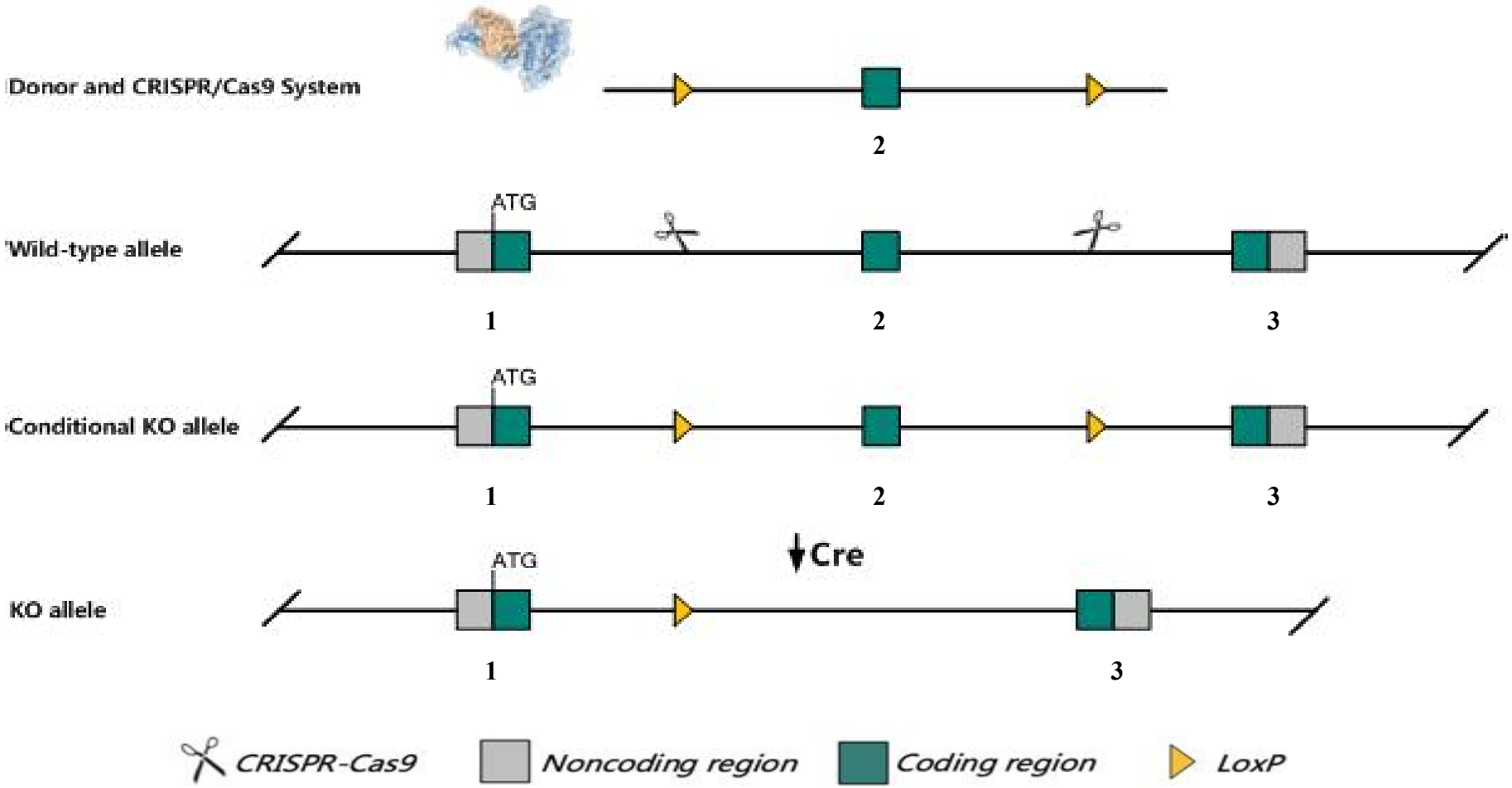
Project Type

- Cas9-CKO

Genetic Background

- C57BL/6JGpt

Strain Strategy



Schematic representation of CRISPR-Cas9 engineering used to edit the *Apoc1* gene.

Technical Information

- The *Apoc1* gene has 4 transcripts. According to the structure of *Apoc1* gene, exon2 of *Apoc1*-202 (ENSMUST00000108451.4) transcript is recommended as the knockout region. The region contains 148bp coding sequence. Knocking out the region will result in disruption of protein function.
- In this project we use CRISPR-Cas9 technology to modify *Apoc1* 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 on-target amplicon sequencing. A stable F1-generation mouse strain was obtained by mating positive F0-generation mice with C57BL/6JGpt mice and confirmation of the desired mutant allele was carried out by PCR and on-target amplicon sequencing.
- 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.

Gene Information

Apoc1 apolipoprotein C-I [Mus musculus (house mouse)]

Gene ID: 11812, updated on 13-Mar-2020

Summary

Official Symbol	Apoc1 provided by MGI
Official Full Name	apolipoprotein C-I provided byMGI
Primary source	MGI:MGI:88053
See related	Ensembl:ENSMUSG00000040564
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	Apo-CIB, ApoC-IB, apo-CI, apoC-I
Summary	This gene encodes a precursor plasma protein that is cleaved to yield a signal peptide and two alternatively processed mature peptides. The encoded protein, which is a component of chylomicrons, very low density lipoproteins and high density lipoproteins, transports lipids from the intestines to other locations in the body. This protein binds to free fatty acids preventing their uptake by cells. This protein is a cofactor for lecithin cholesterol acyltransferase, an enzyme that catalyzes the conversion of free cholesterol to cholesteryl esters. The encoded protein inhibits the activity of the cholesteryl ester transfer protein which promotes the exchange of neutral lipids between lipoproteins. In humans this gene is associated with risk of coronary artery disease and age-associated memory impairment. Mice lacking this gene demonstrate impaired memory. This gene is clustered with three other apolipoprotein genes on chromosome 7. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Dec 2013]
Expression	Biased expression in liver adult (RPKM 1389.4) and liver E18 (RPKM 245.3)See more
Orthologs	human all

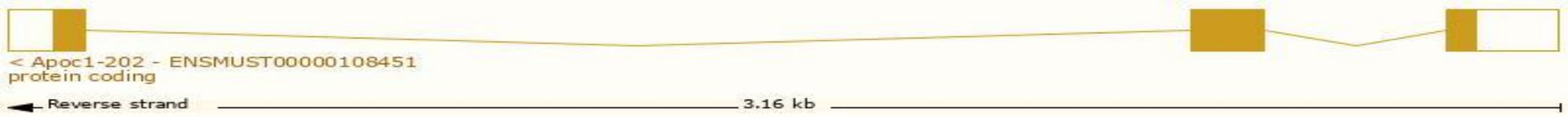
Source: https://www.ncbi.nlm.nih.gov/

Transcript Information

The gene has 4 transcripts,all transcripts are shown below:

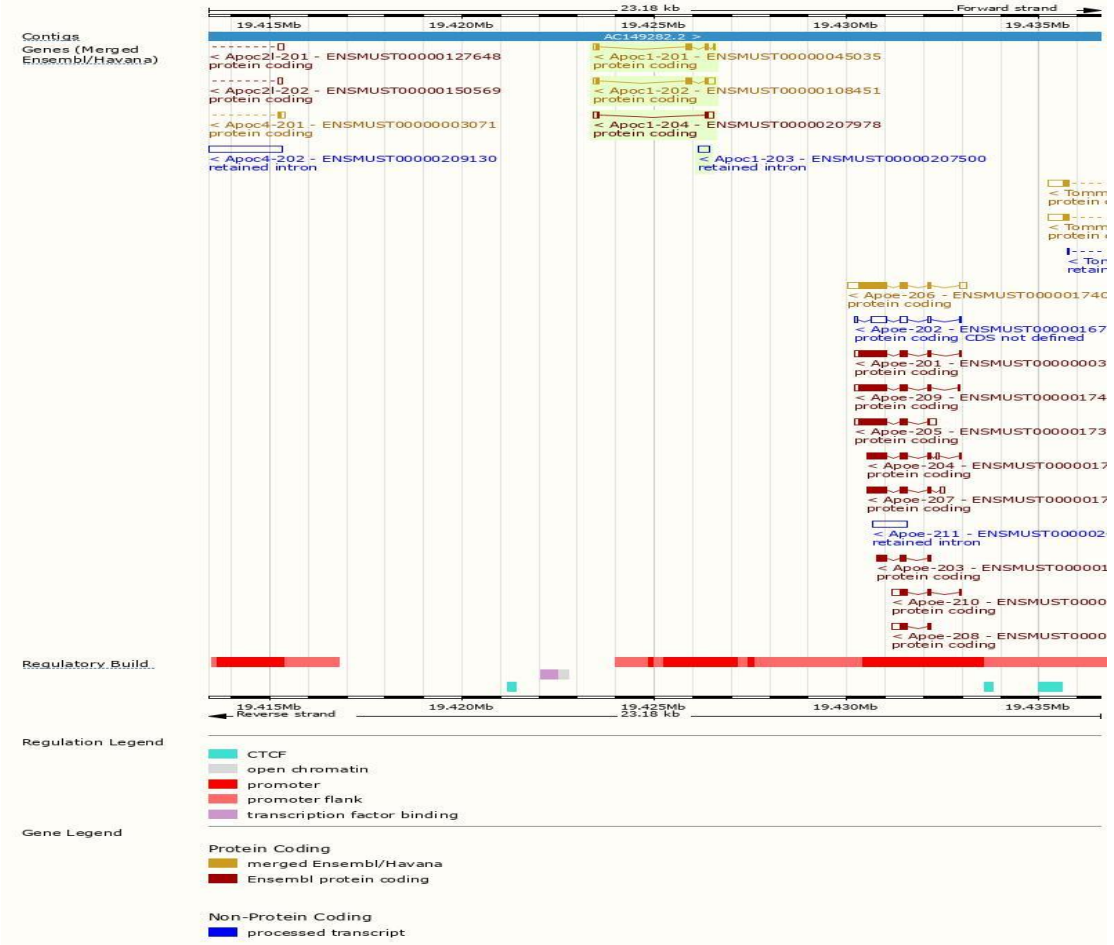
Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Apoc1-202	ENSMUST00000108451.3	532	88aa	Protein coding	CCDS39802	P34928	TSL:1 GENCODE basic APPRIS P1
Apoc1-201	ENSMUST00000045035.11	432	88aa	Protein coding	CCDS39802	P34928	TSL:1 GENCODE basic APPRIS P1
Apoc1-204	ENSMUST00000207978.1	339	29aa	Protein coding	-	A0A140LIY8	TSL:3 GENCODE basic
Apoc1-203	ENSMUST00000207500.1	271	No protein	Retained intron	-	-	TSL:NA

The strategy is based on the design of *Apoc1*-202 transcript, the transcription is shown below:



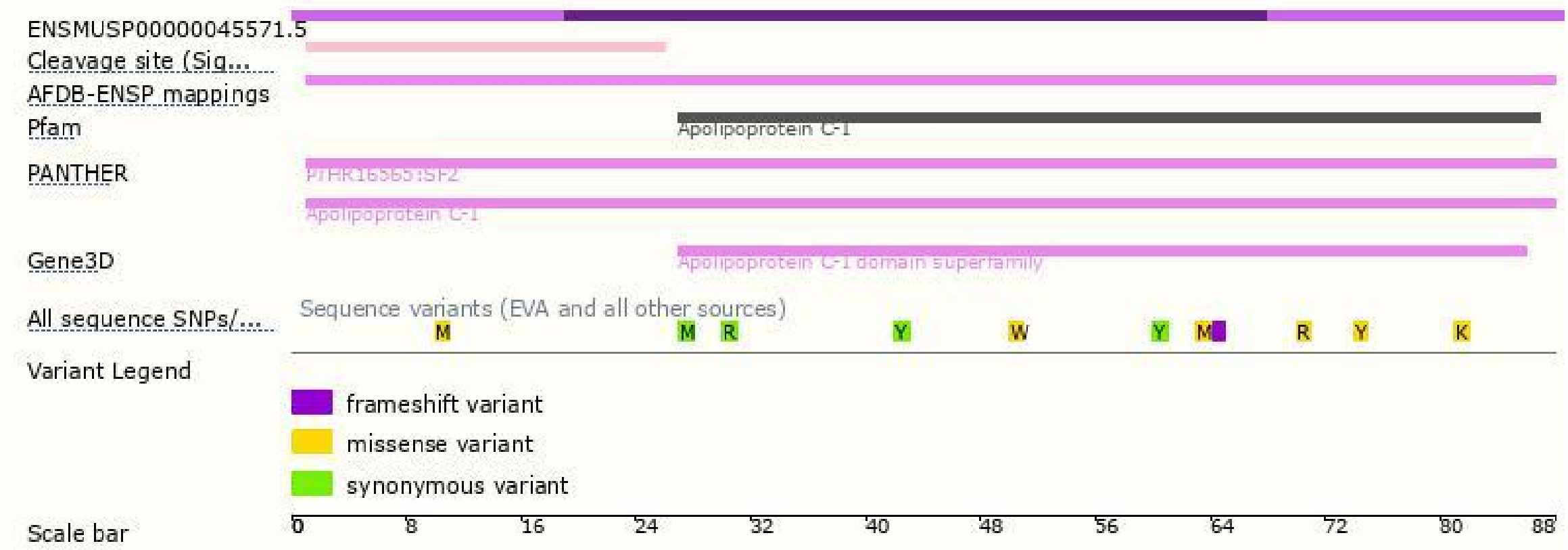
Source: https://www.ensembl.org

Genomic Information



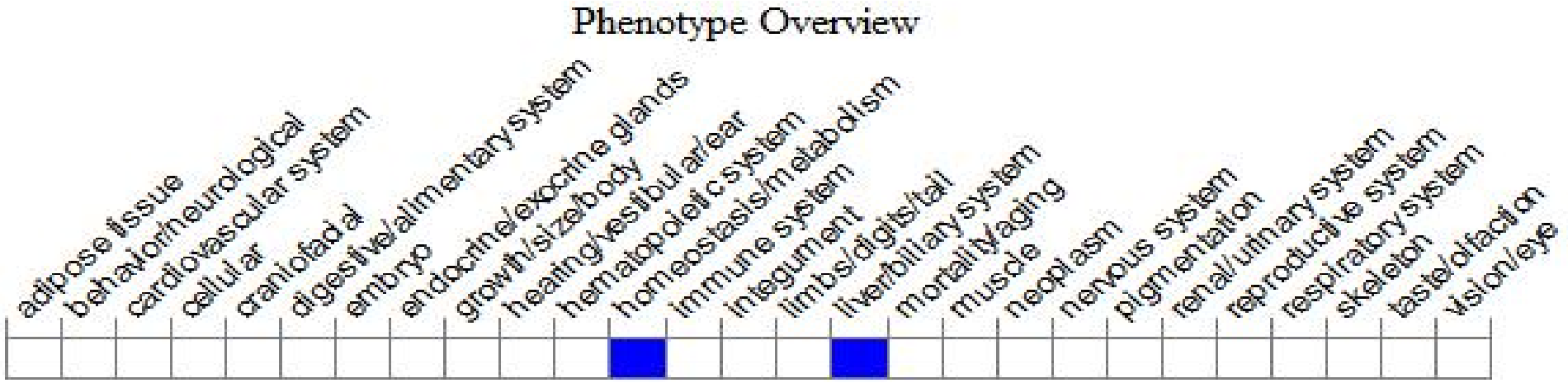
Source: : https://www.ensembl.org

Protein Information



Source: : https://www.ensembl.org

Mouse Phenotype Information (MGI)



- Mice homozygous for a knock-out allele exhibit normal serum lipid levels on a chow diet, develop hypercholesterolemia only when fed a high-fat/high-cholesterol diet, and show significant increases in the liver content of cholesteryl esters and triglycerides and in biliary cholesterol concentration.

Source: https://www.informatics.jax.org

Important Information

- The effect on *Apoc1*-203 is unknwon.
- The intron 1-2 is 375 bp, the loxp insertion may affect the regulation of *Apoc1* gene.
- *Apoc1* is located on Chr7. If the knockout mice are crossed with other mouse strains to obtain double homozygous mutant offspring, please avoid the situation that the second gene is 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 the existing technology level.