Timp1 Cas9-CKO Strategy

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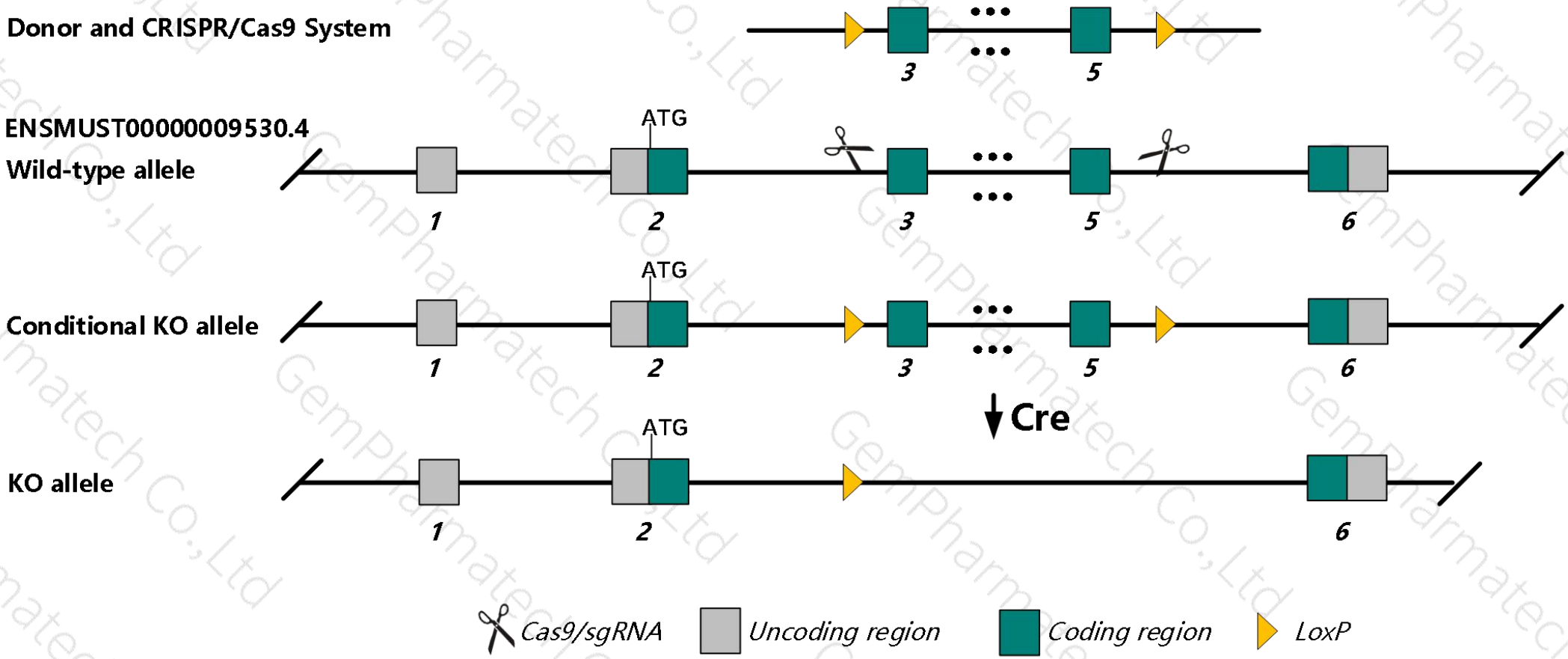
Project Overview

Project Name	***Timp1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Timp1* gene. The schematic diagram is as follows:



Technical routes

- The *Timp1* gene has 2 transcripts. According to the structure of *Timp1* gene, exon3-exon5 of *Timp1-201* (ENSMUST00000009530.4) transcript is recommended as the knockout region.The region contains 332bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Timp1* 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, Nullizygous mice show altered endometrial gland number and estrous cycles, increased uterus and testis weight, reduced female fertility, aortic aneurysms, reduced bone marrow cellularity and susceptibility to bacterial infection, and altered response to myocardium infarction and induced lung injury.

➢ The *Timp1* gene is located on the ChrX. 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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Timp1 tissue inhibitor of metalloproteinase 1 [*Mus musculus* (house mouse)]

Gene ID: 21857, updated on 23-Jul-2019

Summary

Official Symbol	Timp1 provided by MGI
Official Full Name	tissue inhibitor of metalloproteinase 1 provided by MGI
Primary source	MGI:MGI:98752
See related	Ensembl:ENSMUSG00000001131
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	EPA; Clgi; Timp; TIMP-1; TPA-S1
Expression	Biased expression in ovary adult (RPKM 113.3), adrenal adult (RPKM 13.6) and 5 other tissues See more
Orthologs	human all

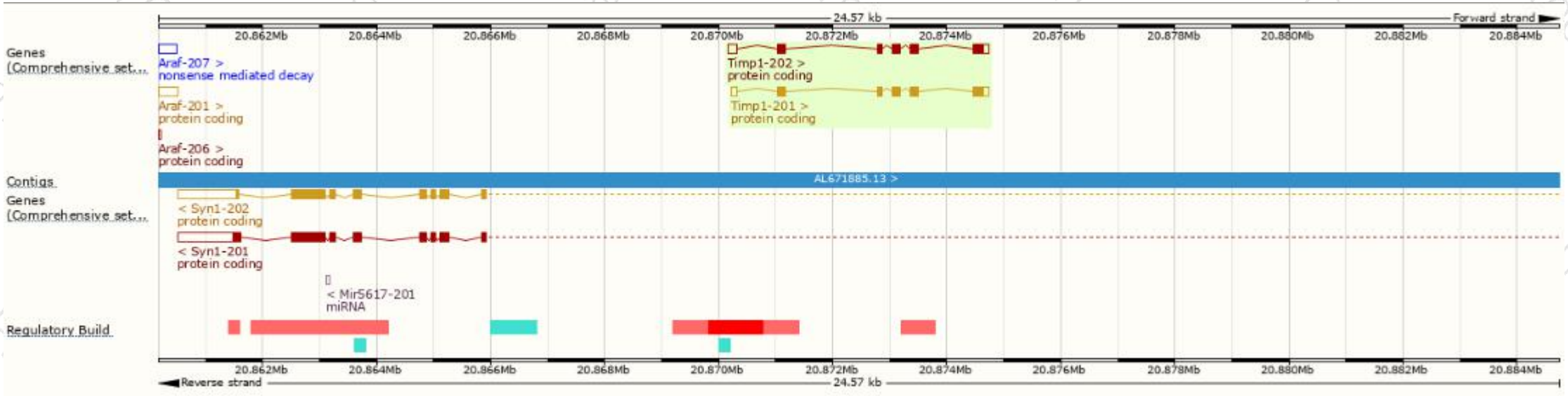
Transcript information（Ensembl）

The gene has 2 transcripts,all transcripts are shown below:

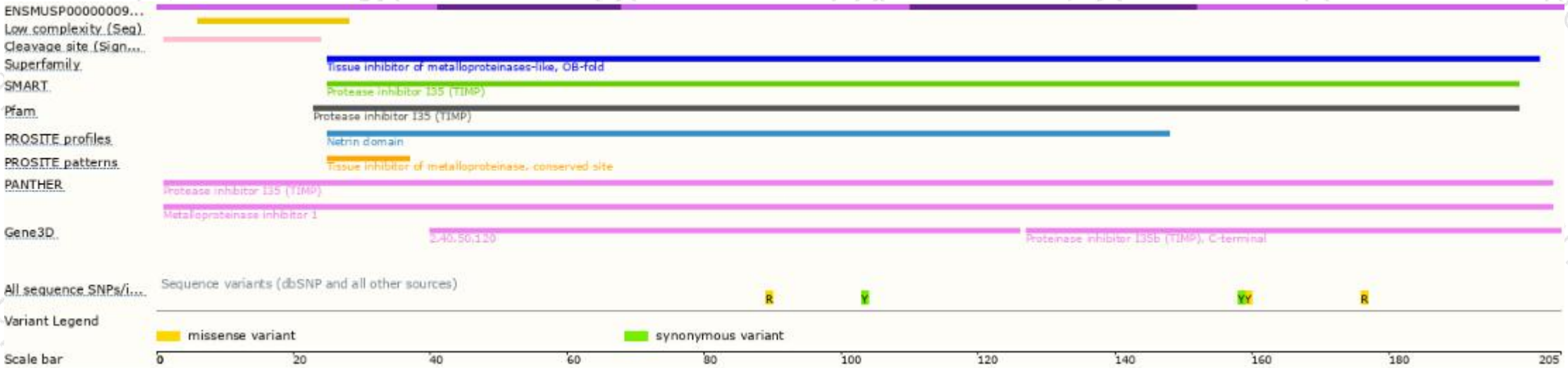
Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Timp1-202	ENSMUST00000115342.9	883	205aa	Protein coding	CCDS30046	P12032	TSL:1 GENCODE basic APPRIS P1
Timp1-201	ENSMUST00000009530.4	833	205aa	Protein coding	CCDS30046	P12032	TSL:1 GENCODE basic APPRIS P1

The strategy is based on the design of *Timp1-201* transcript,The transcription is shown below

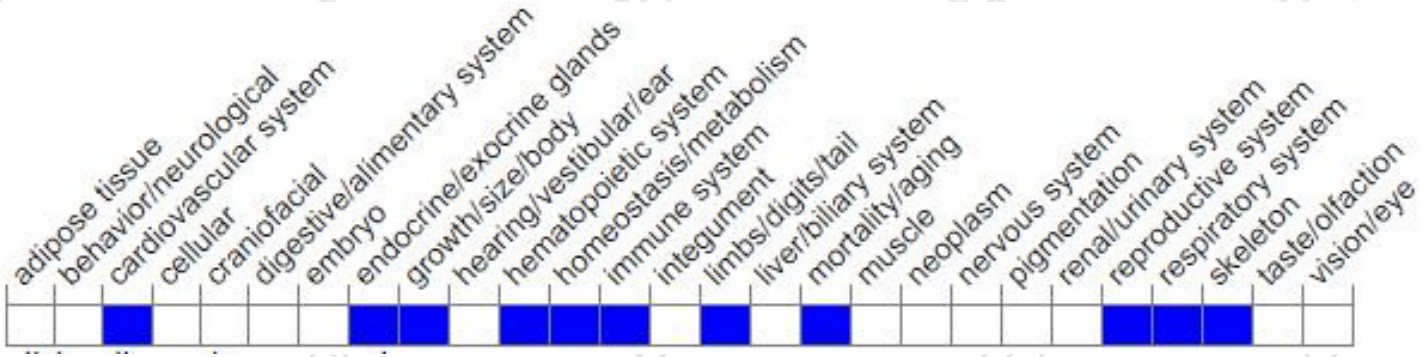
Genomic location distribution



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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