Kcnh1 Cas9-CKO Strategy

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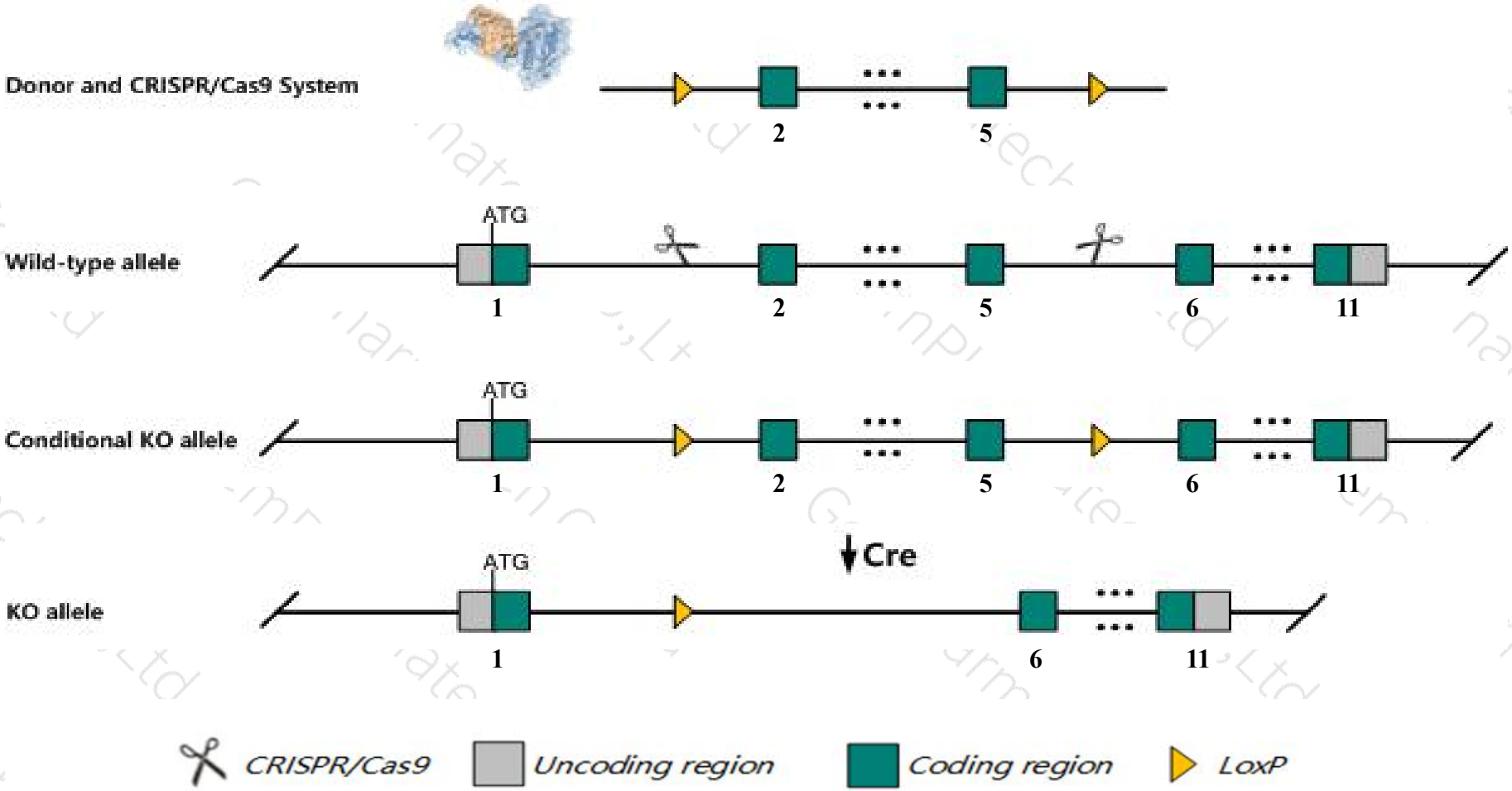
Design Date: 2020-1-31

Project Overview

Project Name	***Kcnh1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Kcnh1* gene. The schematic diagram is as follows:



Technical routes

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- The *Kcnh1* gene has 3 transcripts. According to the structure of *Kcnh1* gene, exon2-exon5 of *Kcnh1-201* (ENSMUST00000078470.11) transcript is recommended as the knockout region.The region contains 479bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Kcnh1* 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,Homozygous mutant mice exhibit a decreased depressive-like response during tail suspension testing. Mice homozygous for a different knock-out allele exhibit longer latency to move in haloperidol-treated mice and mild hyperactivity.

➢ Transcript *Kcnh1-203* may not be affected.

➢ The *Kcnh1* gene is located on the Chr1. 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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Kcnh1 potassium voltage-gated channel, subfamily H (eag-related), member 1 [Mus musculus (house mouse)]

Gene ID: 16510, updated on 31-Jan-2019

Summary

Official Symbol	Kcnh1 provided by MGI
Official Full Name	potassium voltage-gated channel, subfamily H (eag-related), member 1 provided by MGI
Primary source	MGI:MGI:1341721
See related	Ensembl:ENSMUSG00000058248
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	EAG1, Kv10.1, M-eag
Expression	Biased expression in cortex adult (RPKM 6.6), frontal lobe adult (RPKM 5.5) and 9 other tissues See more
Orthologs	human all

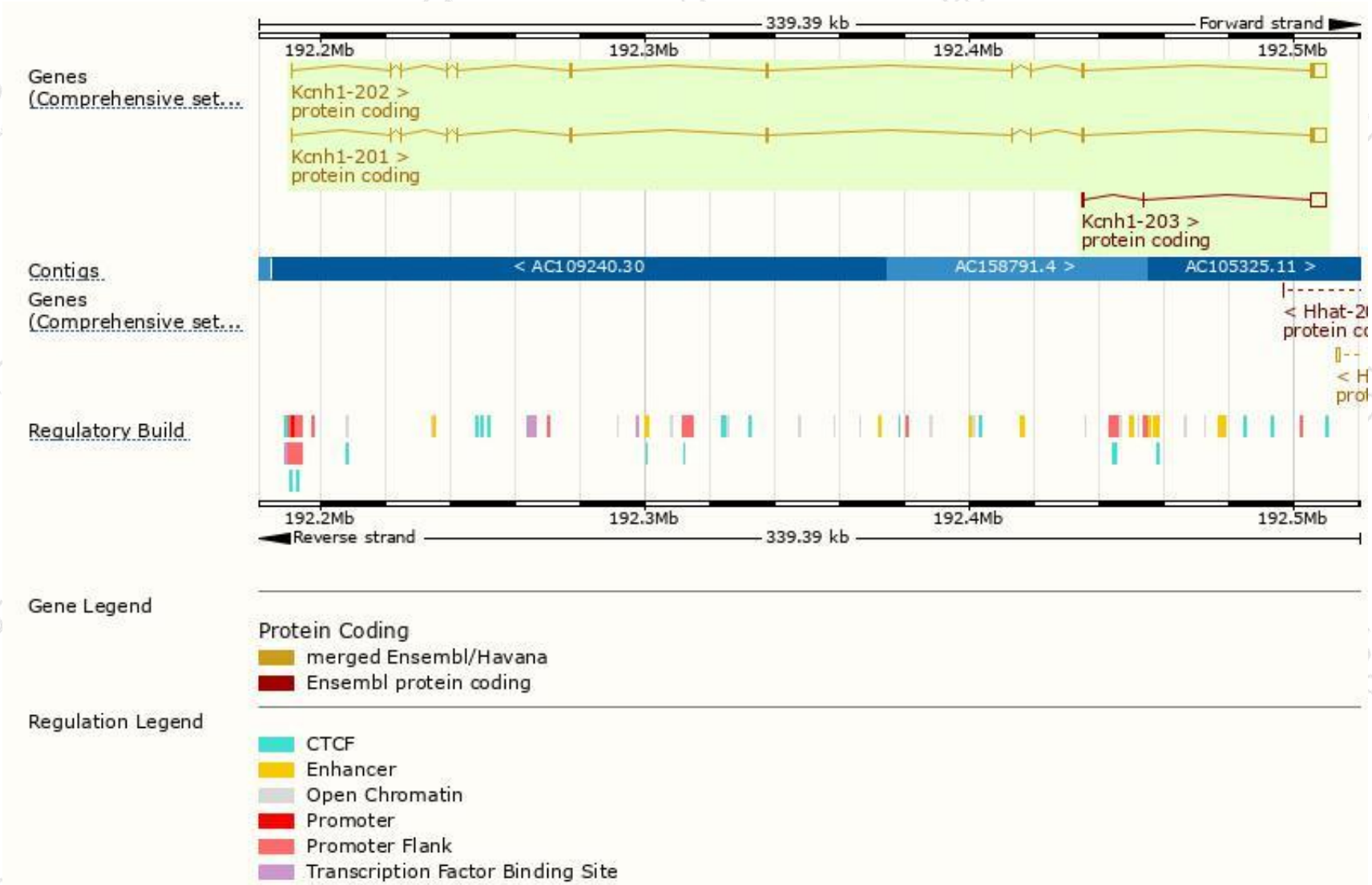
Transcript information（Ensembl）

The gene has 3 transcripts,all transcripts are shown below:

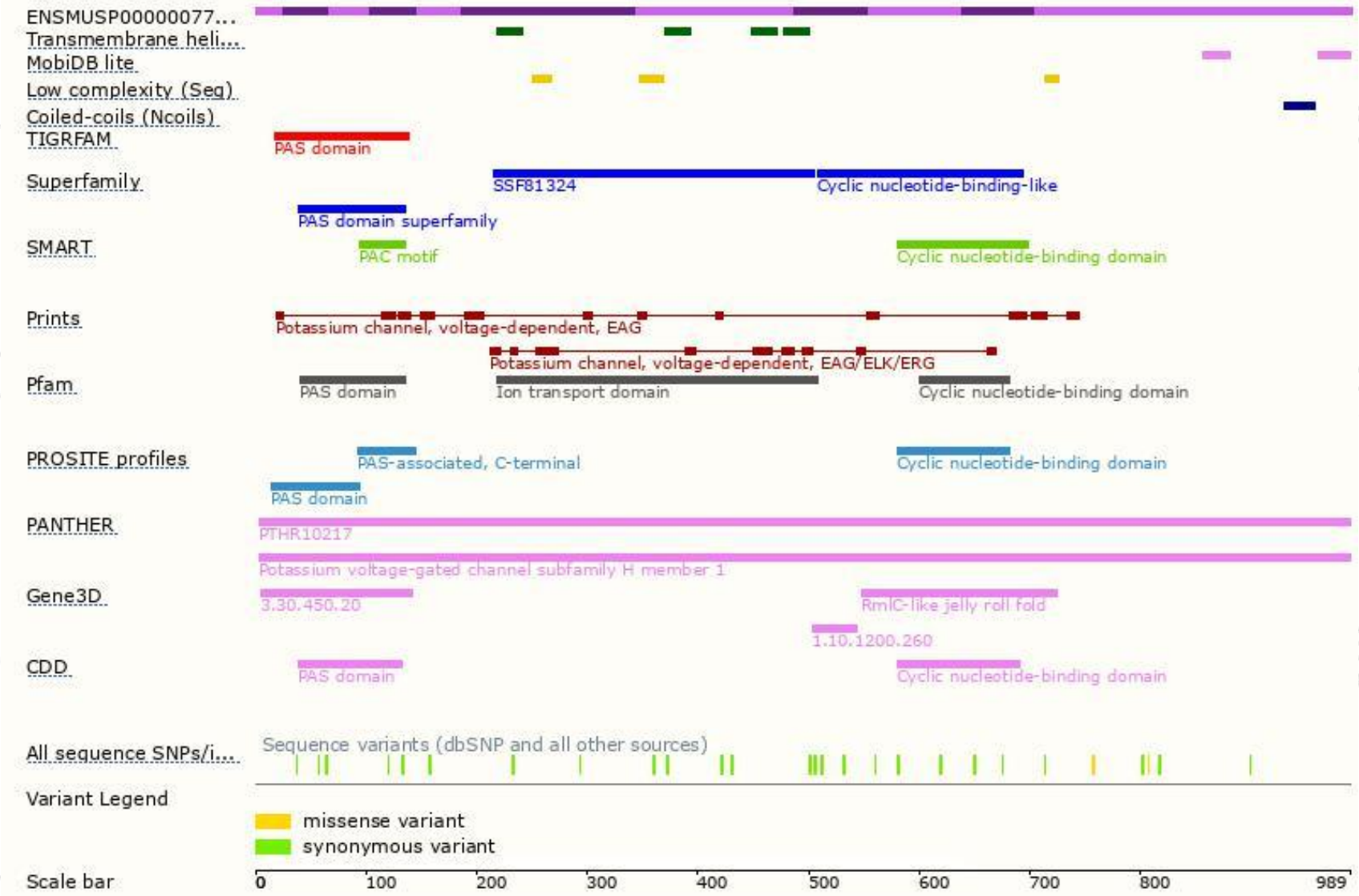
Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Kcnh1-201	ENSMUST00000078470.11	7242	989aa	Protein coding	CCDS15627	A0A1L1M1J8	TSL:1 GENCODE basic APPRIS P3
Kcnh1-202	ENSMUST00000110844.2	7161	962aa	Protein coding	CCDS35826	Q3UHC9	TSL:1 GENCODE basic APPRIS ALT2
Kcnh1-203	ENSMUST00000151152.2	5165	98aa	Protein coding	-	A0A0A6YVS8	CDS 5' incomplete TSL:3

The strategy is based on the design of *Kcnh1-201* transcript,The transcription is shown below

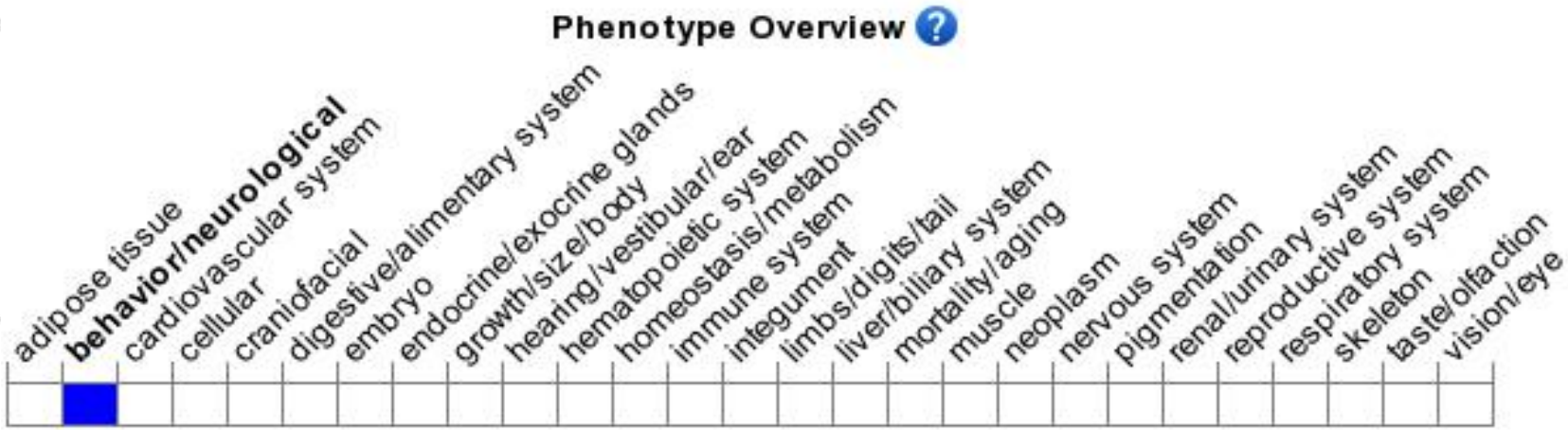
Genomic location distribution



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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