Hgsnat Cas9-KO Strategy

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Reviewer: Xiaojing Li

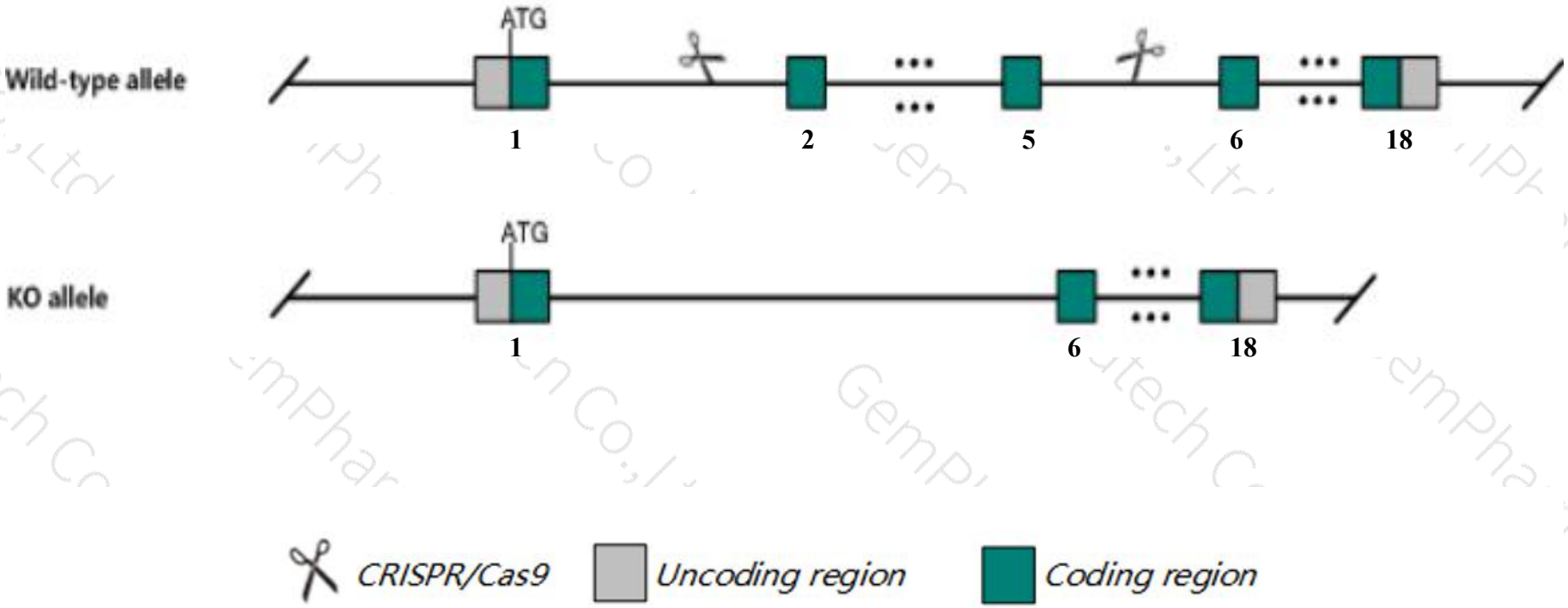
Design Date: 2020-8-1

Project Overview

Project Name	***Hgsnat***
Project type	**Cas9-KO**
Strain background	**C57BL/6JGpt**

Knockout strategy

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



Technical routes

➢ The *Hgsnat* gene has 4 transcripts. According to the structure of *Hgsnat* gene, exon2-exon5 of *Hgsnat-201*(ENSMUST00000037609.7) transcript is recommended as the knockout region.The region contains 445bp coding sequence. Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Hgsnat* gene. The brief process is as follows: CRISPR/Cas9 system 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.

Notice

➢ According to the existing MGI data,mice homozygous for a knock-out allele exhibit progressive storage pathology in the CNS and peripheral organs, glycosaminoglycan accumulation in brain and most somatic organs, lysosomal distension and dysfunction, astrocytosis, microgliosis, hepatosplenomegaly, behavioral deficits and premature death.

➢ The *Hgsnat* gene is located on the Chr8. 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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Hgsnat heparan-alpha-glucosaminide N-acetyltransferase [Mus musculus (house mouse)]

Gene ID: 52120, updated on 13-Mar-2020

Summary

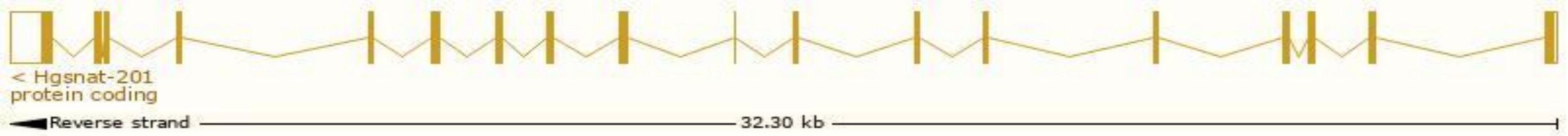
Official Symbol	Hgsnat provided by MGI
Official Full Name	heparan-alpha-glucosaminide N-acetyltransferase provided byMGI
Primary source	MGI:MGI:1196297
See related	Ensembl:ENSMUSG00000037260
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	9430010M12Rik, AW208455, D8Ertd354e, Tmem76
Expression	Ubiquitous expression in cerebellum adult (RPKM 12.4), subcutaneous fat pad adult (RPKM 10.2) and 28 other tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

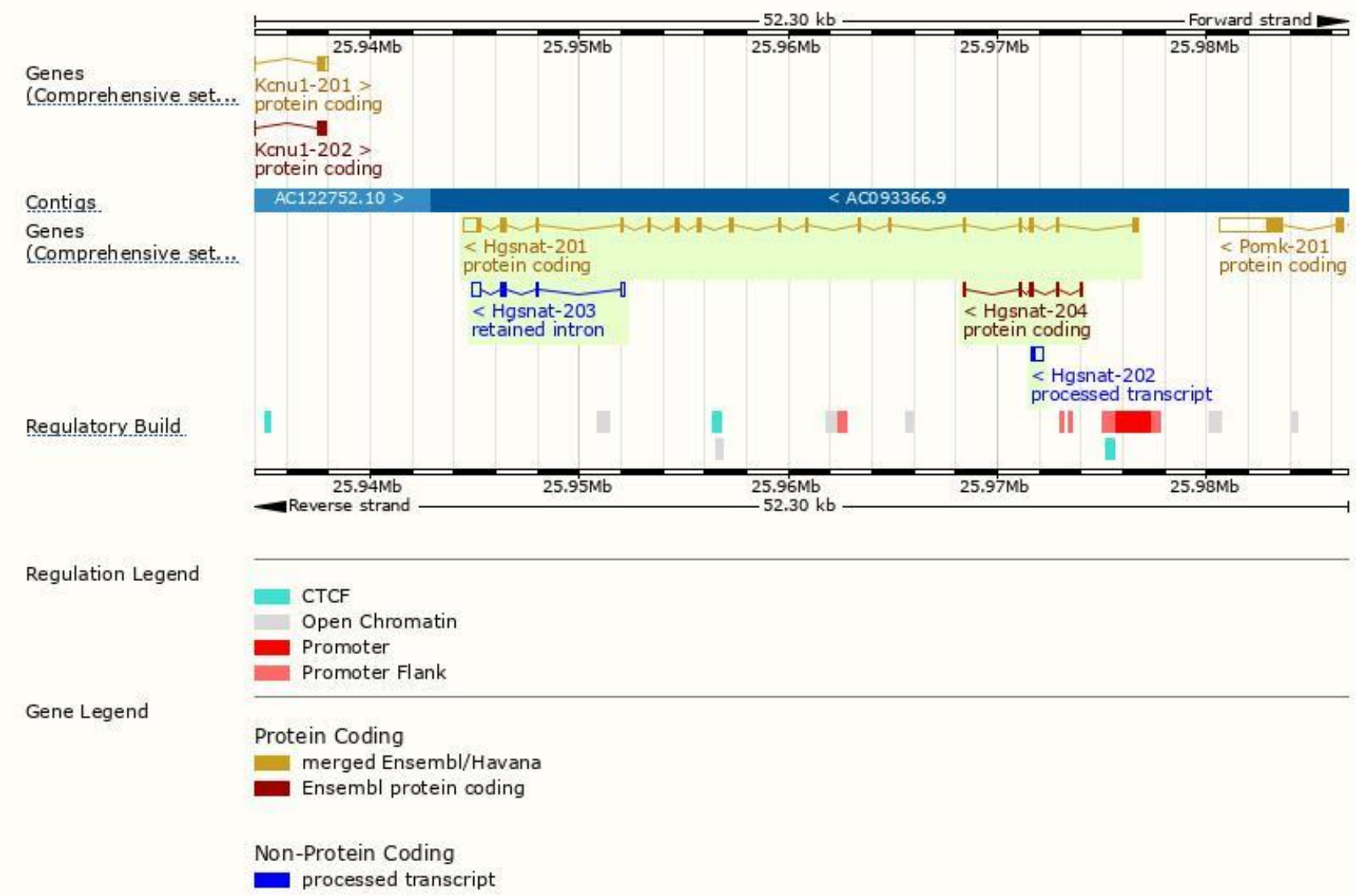
The gene has 4 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Hgsnat-201	ENSMUST00000037609.7	2694	656aa	Protein coding	CCDS40309	Q3UDW8	TSL:1 GENCODE basic APPRIS P1
Hgsnat-204	ENSMUST00000211550.1	485	119aa	Protein coding	-	A0A1B0GRV1	CDS 3' incomplete TSL:5
Hgsnat-202	ENSMUST00000209420.1	489	No protein	Processed transcript	-	-	TSL:3
Hgsnat-203	ENSMUST00000210894.1	870	No protein	Retained intron	-	-	TSL:2

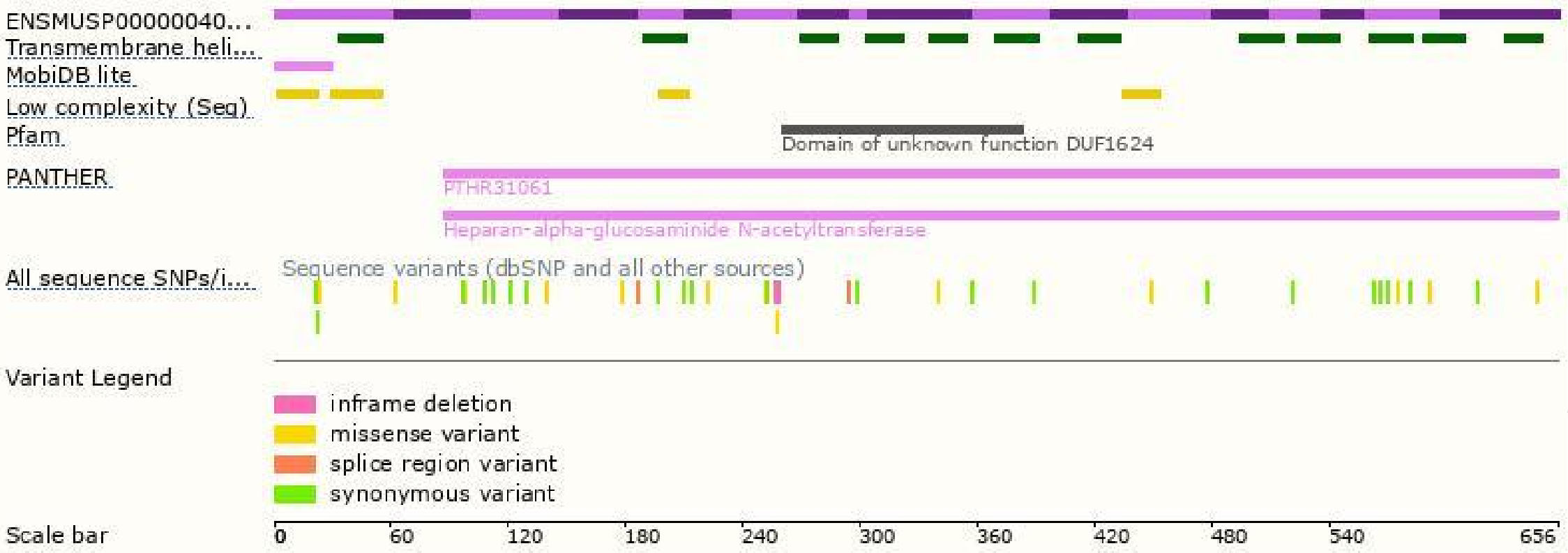
The strategy is based on the design of *Hgsnat-201* transcript,the transcription is shown below:



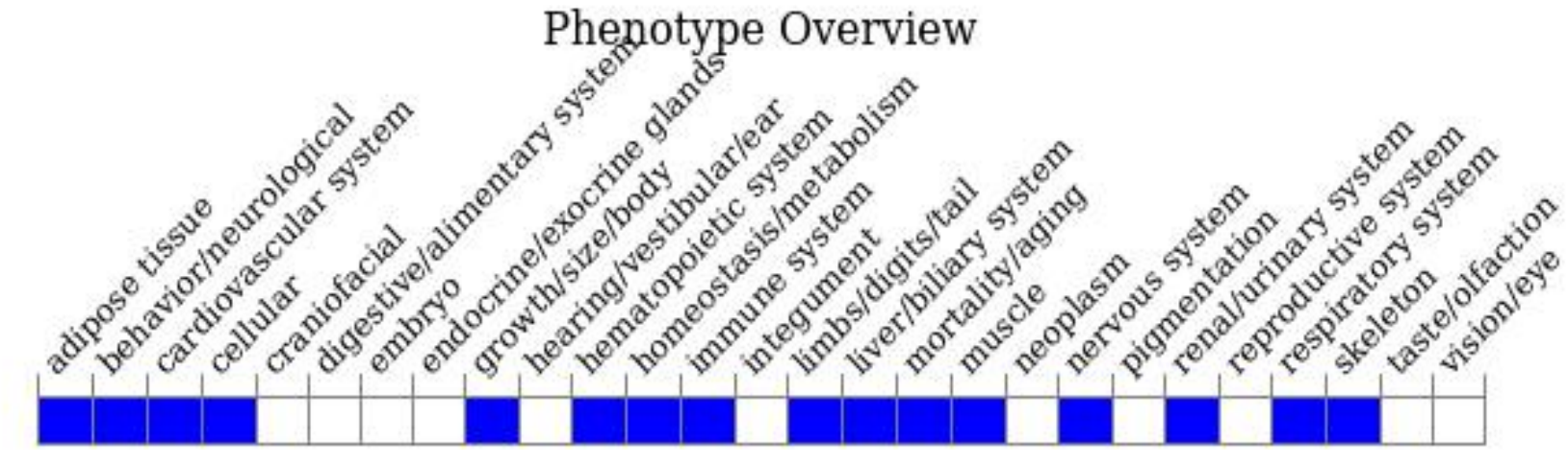
Genomic location distribution



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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