Atxn7l3 Cas9-KO Strategy

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Reviewer: Fengjuan Wang

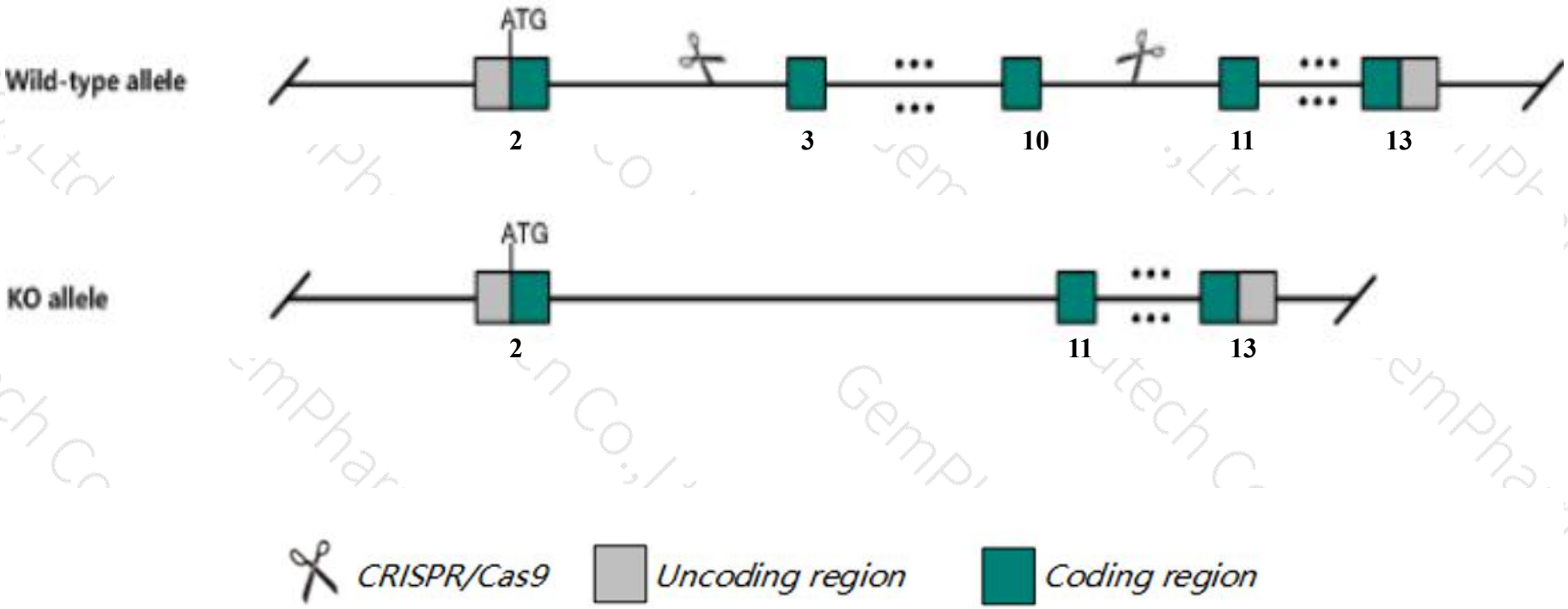
Design Date: 2018-10-17

Project Overview

Project Name	***Atxn7l3***
Project type	**Cas9-KO**
Strain background	**C57BL/6JGpt**

Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Atxn7l3* gene. The schematic diagram is as follows:



Technical routes

➢ The *Atxn7l3* gene has 6 transcripts. According to the structure of *Atxn7l3* gene, exon3-exon10 of *Atxn7l3-201*(ENSMUST00000073234.8) transcript is recommended as the knockout region.The region contains 614bp coding sequence. Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Atxn7l3* 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,mouse embryonic stem cells homozygous for a knock-out allele exhibit strikingly increased H2B monoubiquitination (H2Bub) levels and fail to show loss of global H2Bub following inhibition of transcriptional elongation.

➢ The Intron2 and Intron10 are only 306bp and 234bp,loxp insertion may affect mRNA splicing.

➢ The *Atxn7l3* gene is located on the Chr11. 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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Atxn7l3 ataxin 7-like 3 [Mus musculus (house mouse)]

Gene ID: 217218, updated on 13-Mar-2020

Summary

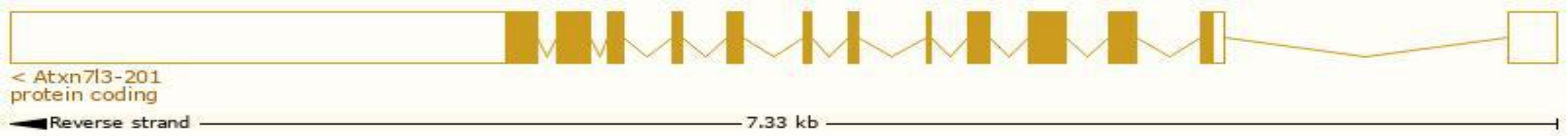
Official Symbol	Atxn7l3 provided by MGI
Official Full Name	ataxin 7-like 3 provided byMGI
Primary source	MGI:MGI:3036270
See related	Ensembl:ENSMUSG00000059995
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	E030022H21Rik
Expression	Ubiquitous expression in cortex adult (RPKM 32.3), whole brain E14.5 (RPKM 28.1) and 28 other tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

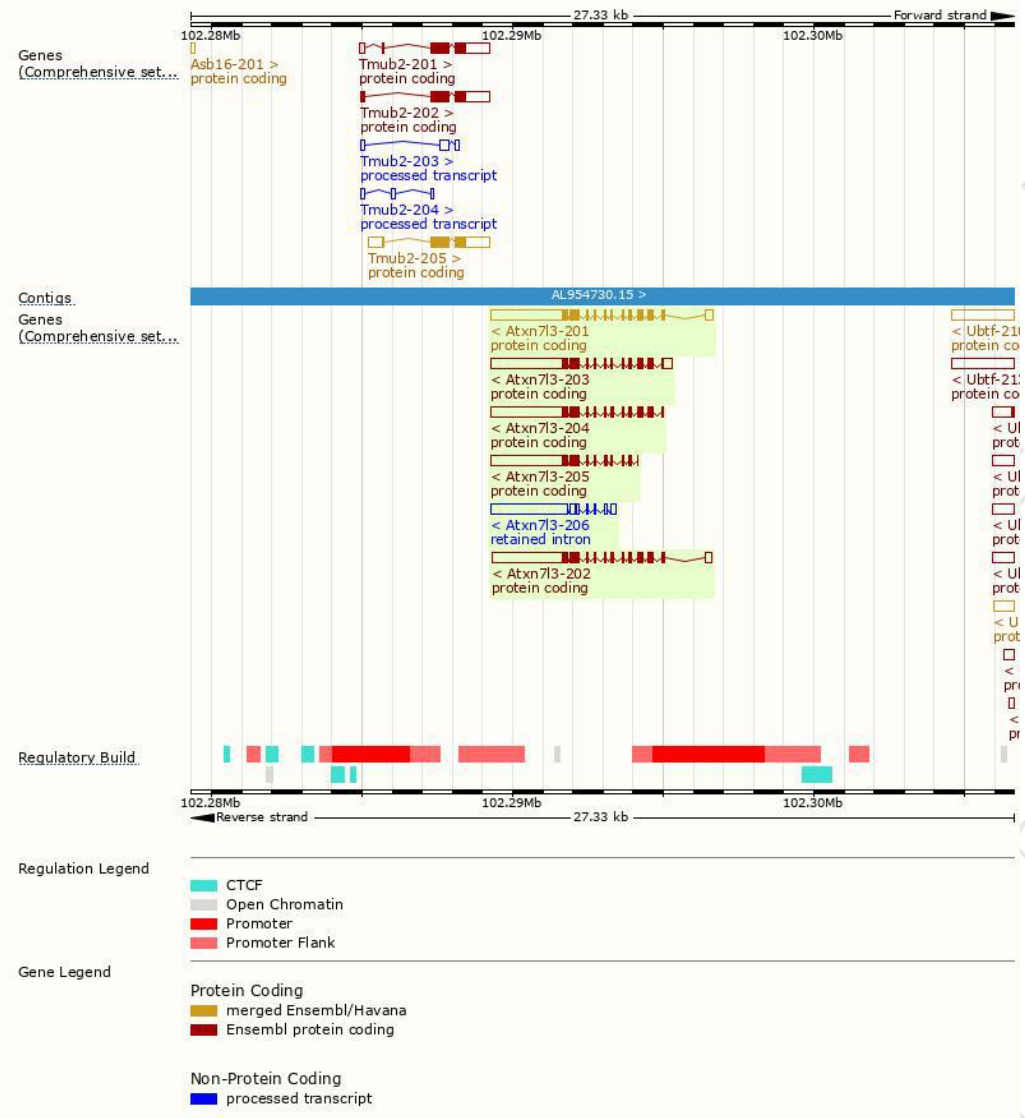
The gene has 6 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Atxn7l3-203	ENSMUST00000107134.7	3712	347aa	Protein coding	CCDS48941	A2AWT3	TSL:5 GENCODE basic APPRIS ALT1
Atxn7l3-202	ENSMUST00000107132.2	3706	354aa	Protein coding	CCDS48942	A2AWT3	TSL:5 GENCODE basic APPRIS P4
Atxn7l3-201	ENSMUST00000073234.8	3688	347aa	Protein coding	CCDS48941	A2AWT3	TSL:1 GENCODE basic APPRIS ALT1
Atxn7l3-204	ENSMUST00000137387.7	3408	350aa	Protein coding	-	Z4YN62	CDS 5' incomplete TSL:5
Atxn7l3-205	ENSMUST00000141516.7	3130	258aa	Protein coding	-	F6RCN9	CDS 5' incomplete TSL:5
Atxn7l3-206	ENSMUST00000145484.1	3102	No protein	Retained intron	-	-	TSL:1

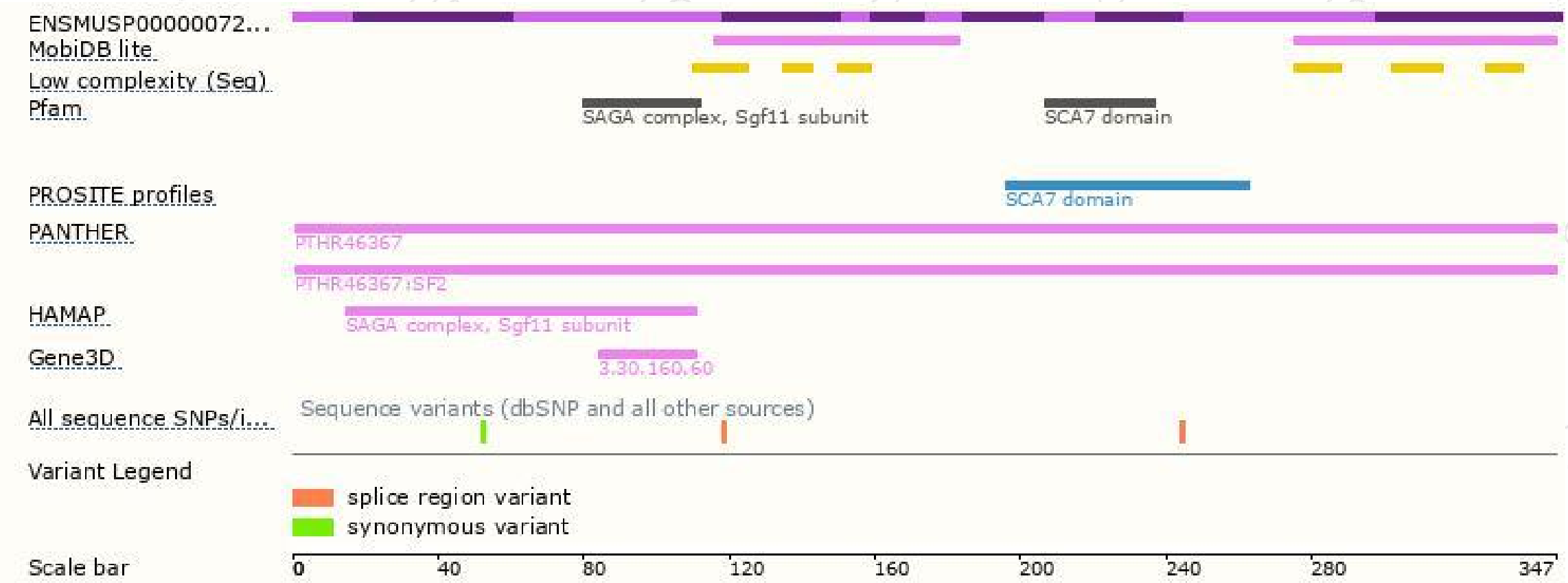
The strategy is based on the design of *Atxn7l3-201* transcript,the transcription is shown below:



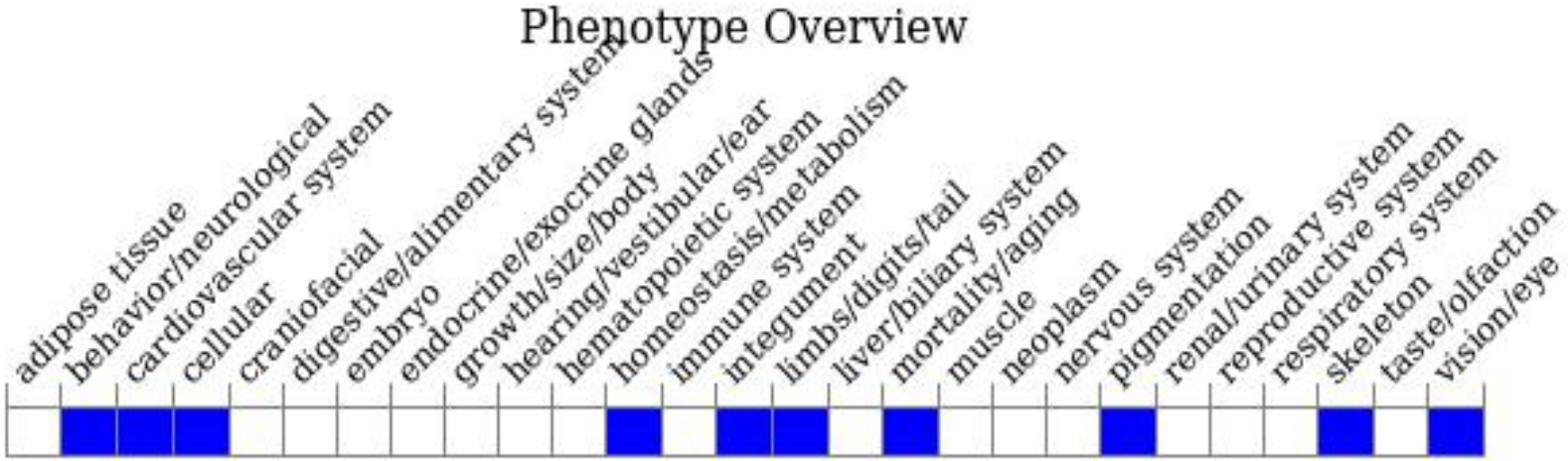
Genomic location distribution



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,mouse embryonic stem cells homozygous for a knock-out allele exhibit strikingly increased H2B monoubiquitination (H2Bub) levels and fail to show loss of global H2Bub following inhibition of transcriptional elongation.

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

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