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Suv39h1 Cas9-CKO Strategy

Designer: Shanhong Tao

Reviewer: Linyan Wu

Design Date: 2024-03-08

Overview

Target Gene Name

- Suv39h1

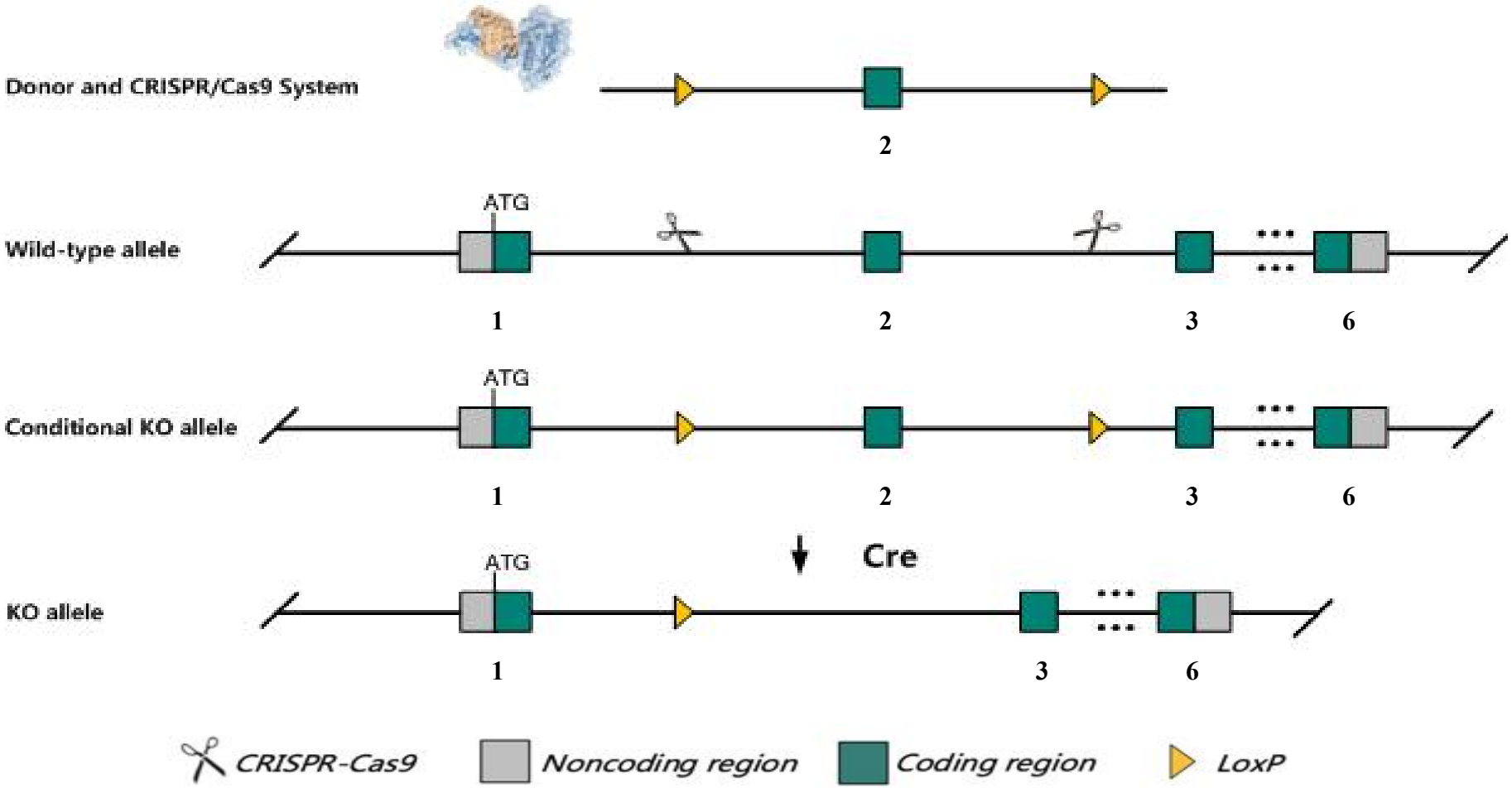
Project Type

- Cas9-CKO

Genetic Background

- C57BL/6JGpt

Strain Strategy



Schematic representation of CRISPR-Cas9 engineering used to edit the *Suv39h1* gene.

Technical Information

- The *Suv39h1* gene has 5 transcripts. According to the structure of *Suv39h1* gene, exon2 of *Suv39h1*-203 (ENSMUST00000115638.10) transcript is recommended as the knockout region. The region contains 146bp coding sequence. Knocking out the region will result in disruption of protein function.
- In this project we use CRISPR-Cas9 technology to modify *Suv39h1* 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

Suv39h1 suppressor of variegation 3-9 1 [*Mus musculus* (house mouse)]

Download Datasets

Gene ID: 20937, updated on 5-Mar-2024

Summary

Official Symbol	Suv39h1 provided by MGI
Official Full Name	suppressor of variegation 3-9 1 provided by MGI
Primary source	MGI:MGI:1099440
See related	Ensembl:ENSMUSG00000039231 AllianceGenome:MGI:1099440
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	mIS6; KMT1A; DXHXS7466e; H3-K9-HMTase 1
Summary	Enables RNA polymerase II transcription regulatory region sequence-specific DNA binding activity and histone methyltransferase activity (H3-K9 specific). Involved in histone H3-K9 methylation; negative regulation of circadian rhythm; and negative regulation of transcription, DNA-templated. Acts upstream of or within several processes, including blastocyst hatching; positive regulation of histone H3-K9 trimethylation; and regulation of cellular response to stress. Located in heterochromatin and nucleus. Part of chromatin silencing complex. Is expressed in several structures, including alimentary system; early conceptus; genitourinary system; integumental system; and nervous system. Orthologous to human SUV39H1 (SUV39H1 histone lysine methyltransferase). [provided by Alliance of Genome Resources, Apr 2022]
Expression	Ubiquitous expression in thymus adult (RPKM 16.1), CNS E11.5 (RPKM 15.8) and 28 other tissues See more
Orthologs	human all

NEW **Try the new Gene table**
Try the new Transcript table

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

Transcript Information

The gene has 5 transcripts,all transcripts are shown below:

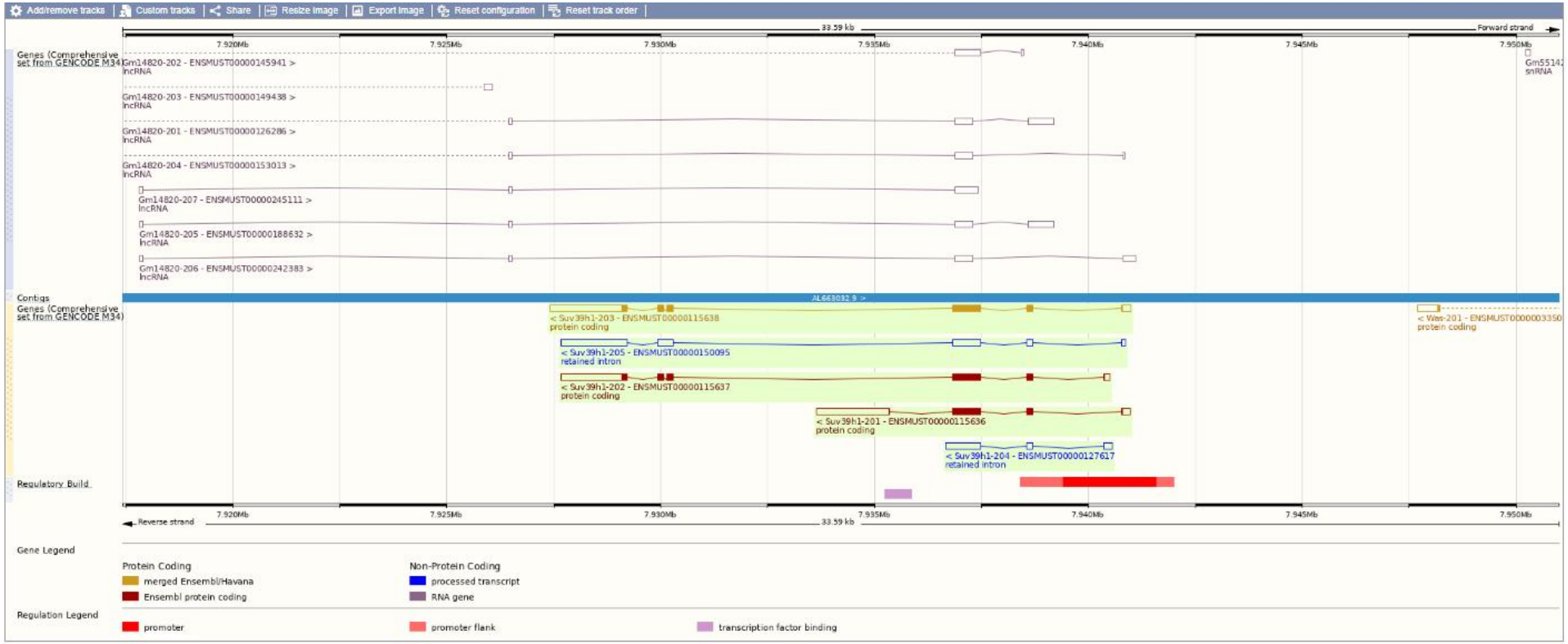
Show/hide columns (1 hidden) Filter

Transcript ID	Name	bp	Protein	Biotype	CCDS	UniProt Match	Flags
ENSMUST00000115637.8	Suv39h1-202	2778	413aa	Protein coding	CCDS72337	A2AC19	Ensembl Canonical GENCODE basic TSL:2
ENSMUST00000115638.10	Suv39h1-203	3116	412aa	Protein coding	CCDS40846	O54864	GENCODE basic APPRIS P1 TSL:1
ENSMUST00000115636.4	Suv39h1-201	2707	286aa	Protein coding		O54864-3	GENCODE basic TSL:1
ENSMUST00000150095.8	Suv39h1-205	2807	No protein	Retained intron		-	TSL:2
ENSMUST00000127617.2	Suv39h1-204	1166	No protein	Retained intron		-	TSL:2

The strategy is based on the design of *Suv39h1*-203 transcript, the transcription is shown below:

Source: https://www.ensembl.org

Genomic Information



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

Protein Information

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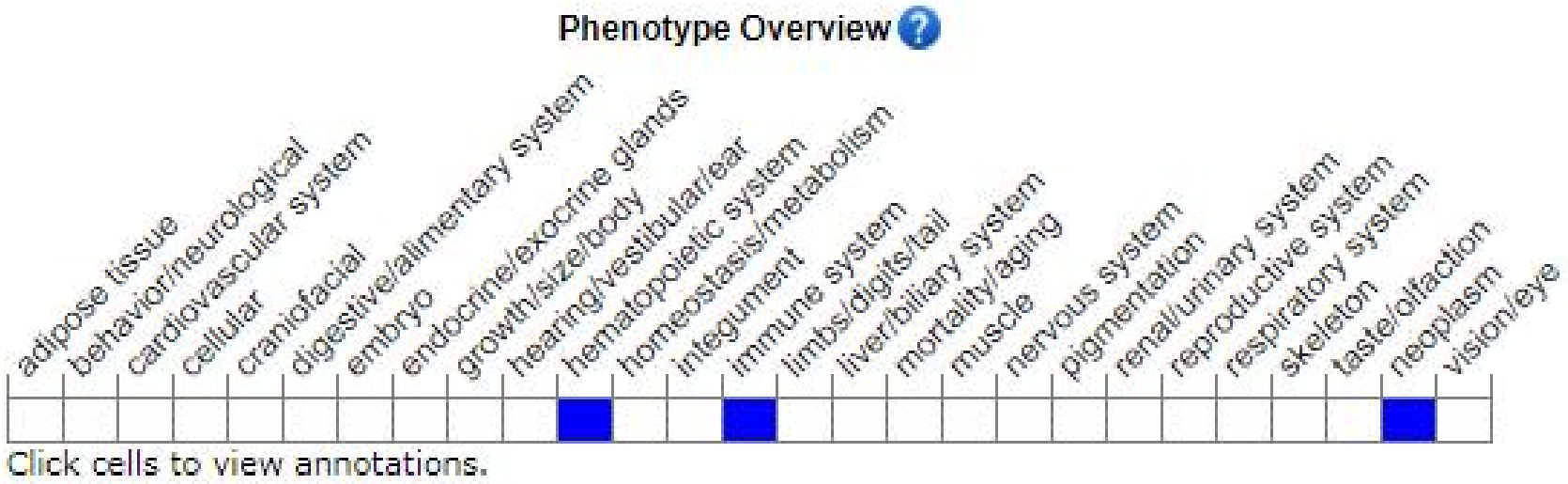
Source: : https://www.ensembl.org

Mouse Phenotype Information (MGI)



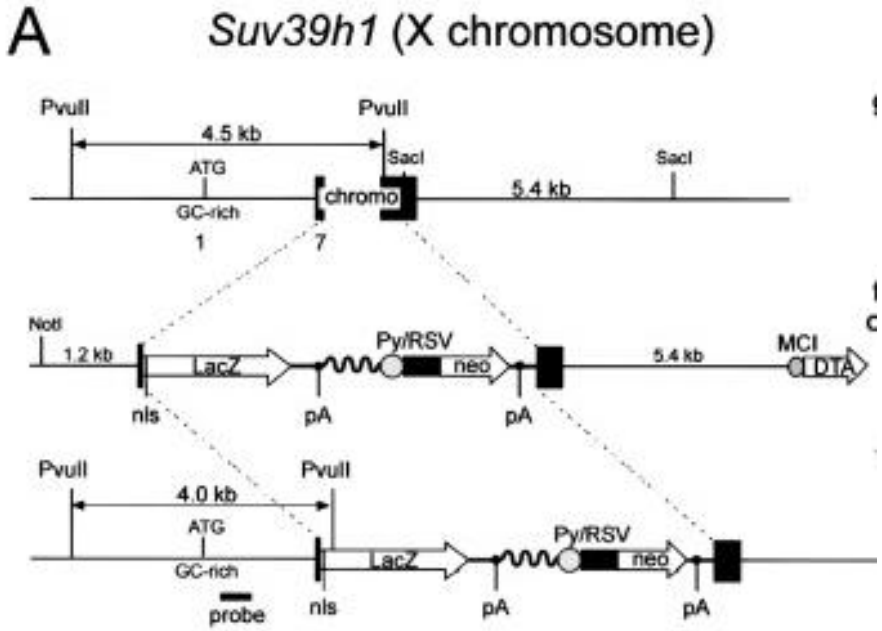
- About one third of mice either heterozygous or homozygous for a reporter/null allele develop late-onset B cell lymphomas.

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

Important Information

- According to the existing MGI data,about one third of mice either heterozygous or homozygous for a reporter/null allele develop late-onset B cell lymphomas.
- The floxed region overlaps with *Gm14820* gene, it will be destroyed.
- The loxp of 5-terminal may be in the promoter region of the *Suv39h1* gene, this strategy may influence the regulatory function of the *Suv39h1* gene.
- *Suv39h1* is located on ChrX. 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.

References



Targeted Disruption of the *Suv39h1* and *Suv39h2* Gene Loci in the Mouse Germline

Murine Suv39h HMTases are encoded by two loci which have been mapped to centromere-proximal positions in the X chromosome (*Suv39h1*) or in chromosome 2 (*Suv39h2*) (O'Carroll et al. 2000). Both gene loci were independently disrupted by homologous recombination in embryonic stem (ES) cells using a conventional targeting approach that replaces parts of the evolutionarily conserved chromo domain with the bacterial *LacZ* gene and an *RSV-neomycin* selecion cassette (Figure 1A). These targeting strategies produce in-frame fusion proteins of the first 40 amino acids of Suv39h1 or of the first 113 amino acids of Suv39h2 with lacZ, which maintain β-galactosidase activities (data not shown). Successfully targeted ES cell clones were used to generate chimeric mice that transmitted the mutated *Suv39h1* or *Suv39h2* alleles through the germline (Figure 1B). Protein blot analyses of testis nuclear extracts from wild-type, *Suv39h1*-, and *Suv39h2*-deficient mice with α-Suv39h1 and α-Suv39h2 specific antibodies (O'Carroll et al. 2000) indicated absence of the respective proteins, demonstrating that we had generated null alleles for both genes (Figure 1C).

(A) Diagrammatic representation of the *Suv39h1* and *Suv39h2* genomic loci, the replacement vectors and the targeted alleles. Exons are indicated by black boxes with numbers referring to the starting amino acid positions of the respective exons (O'Carroll et al., 2000). Also shown are the diagnostic restriction sites and the external probes used for Southern blot analyses.

Peters AH, O'Carroll D, Scherthan H, Mechtler K, Sauer S, Schöfer C, Weipoltshammer K, Pagani M, Lachner M, Kohlmaier A, Opravil S, Doyle M, Sibilia M, Jenuwein T. Loss of the Suv39h histone methyltransferases impairs mammalian heterochromatin and genome stability. Cell. 2001 Nov 2;107(3):323-37. doi: 10.1016/s0092-8674(01)00542-6. PMID: 11701123.