GemPharmatech™

Dchs1 Cas9-KO Strategy

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Reviewer: Yao Yu

Design Date: 2023-12-14

Overview

Target Gene Name

- *Dchs1*

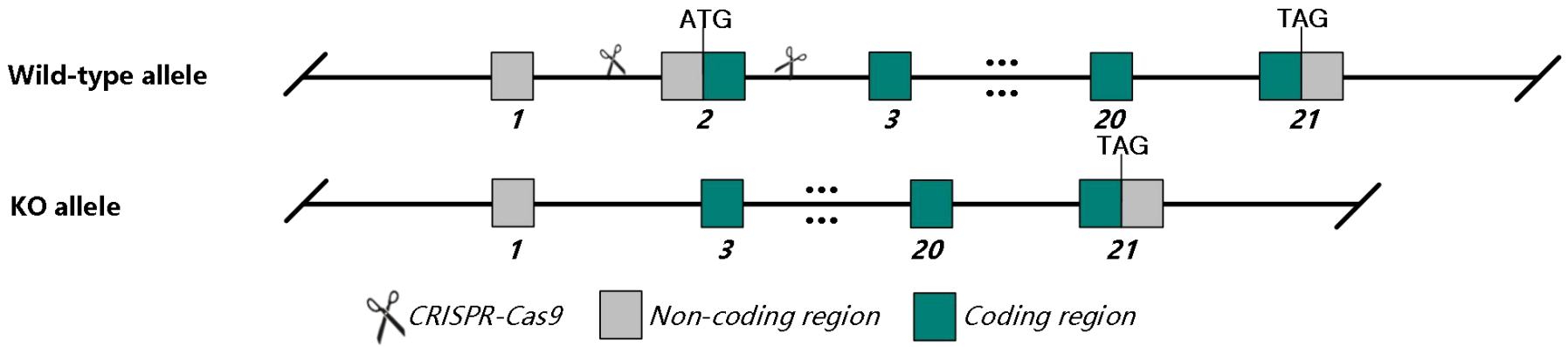
Project Type

- Cas9-KO

Genetic Background

- C57BL/6JGpt

Strain Strategy



Schematic representation of CRISPR-Cas9 engineering used to edit the *Dchs1* gene.

Technical Information

- The *Dchs1* gene has 3 transcripts. According to the structure of *Dchs1* gene, exon 2 of *Dchs1*-201 (ENSMUST00000078482.13) is recommended as the knockout region. The region contains the start codon ATG. Knocking out the region will result in disruption of gene function.
- In this project we use CRISPR-Cas9 technology to modify *Dchs1* gene. The brief process is as follows: gRNAs were transcribed in vitro. Cas9 and gRNAs 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.

Gene Information

Dchs1 dachsous cadherin related 1 [*Mus musculus* (house mouse)]

Download Datasets

Gene ID: 233651, updated on 23-Nov-2023

Summary

Official Symbol	Dchs1 provided by MGI
Official Full Name	dachsous cadherin related 1 provided by MGI
Primary source	MGI:MGI:2685011
See related	Ensembl:ENSMUSG00000036862 AllianceGenome:MGI:2685011
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	FIB1; CDH25; Gm165; PCDH16; 3110041P15Rik; C130033F22Rik
Summary	Predicted to enable cadherin binding activity and calcium ion binding activity. Involved in several processes, including cell migration; heterophilic cell-cell adhesion via plasma membrane cell adhesion molecules; and hippo signaling. Acts upstream of or within several processes, including animal organ development; condensed mesenchymal cell proliferation; and post-anal tail morphogenesis. Located in apical part of cell. Is expressed in several structures, including alimentary system; central nervous system; heart; hemolymphoid system gland; and lung. Used to study mitral valve prolapse. Human ortholog(s) of this gene implicated in Van Maldergem syndrome 1 and mitral valve prolapse. Orthologous to human DCHS1 (dachsous cadherin-related 1). [provided by Alliance of Genome Resources, Apr 2022]
Expression	Broad expression in whole brain E14.5 (RPKM 20.4), limb E14.5 (RPKM 19.1) and 22 other tissues See more
Orthologs	human all

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

Genomic context

Location: 7 E3; 7 55.98 cM — See Dchs1 in Genome Data Viewer

Exon count: 23

https://www.ncbi.nlm.nih.gov/gene/233651

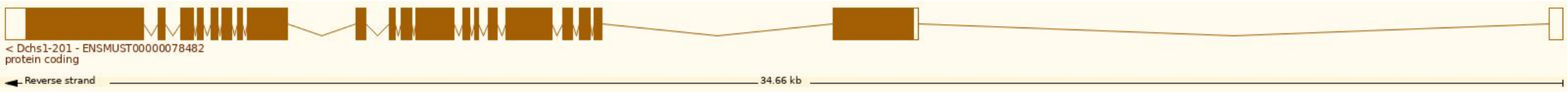
Transcript Information

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

Show/hide columns (1 hidden) Filter

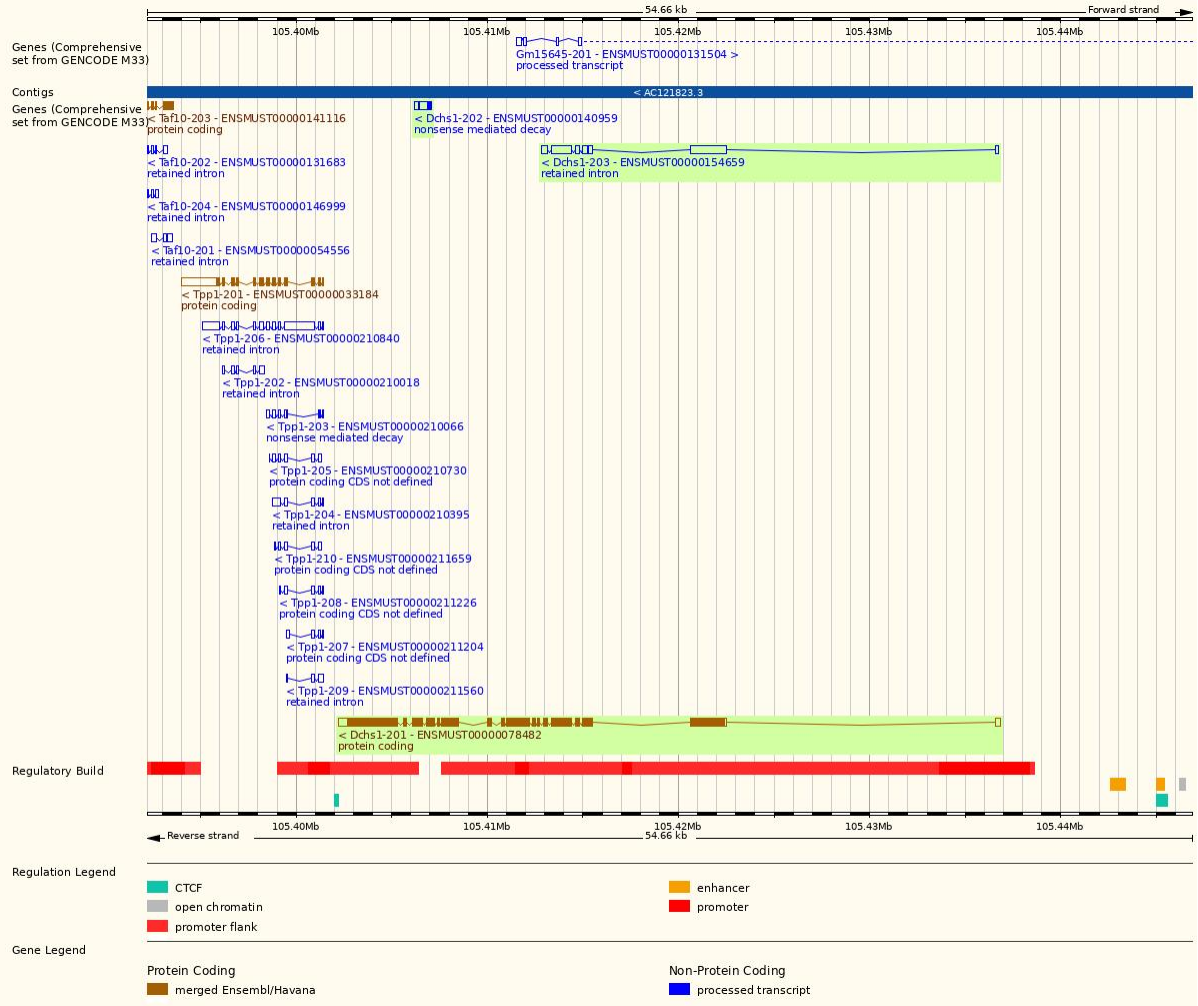
Transcript ID	Name	bp ▼	Protein	Biotype	CCDS	UniProt Match	Flags
ENSMUST00000078482.13	Dchs1-201	10754	3291aa	Protein coding	CCDS52351	E9PVD3	Ensembl Canonical, GENCODE basic, APPRIS P1, TSL:5
ENSMUST00000154659.2	Dchs1-203	4073	No protein	Retained intron		-	TSL:1
ENSMUST00000140959.2	Dchs1-202	743	50aa	Nonsense mediated decay		A0A1B0GSA3	TSL:3, CDS 5' incomplete

The strategy is based on the design of *Dchs1*-201 transcript, the transcription is shown below:



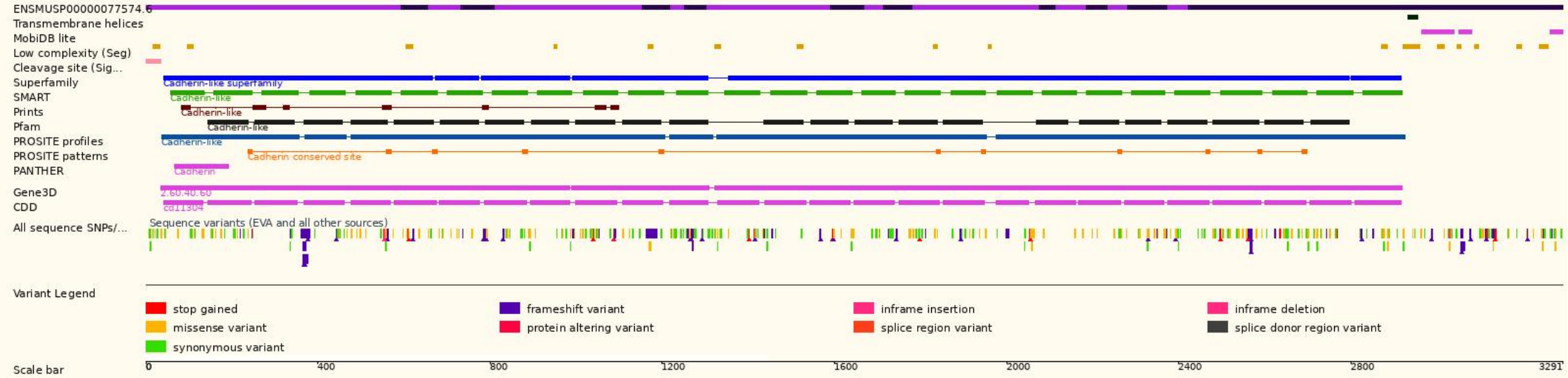
Source: http://asia.ensembl.org/

Genomic Information



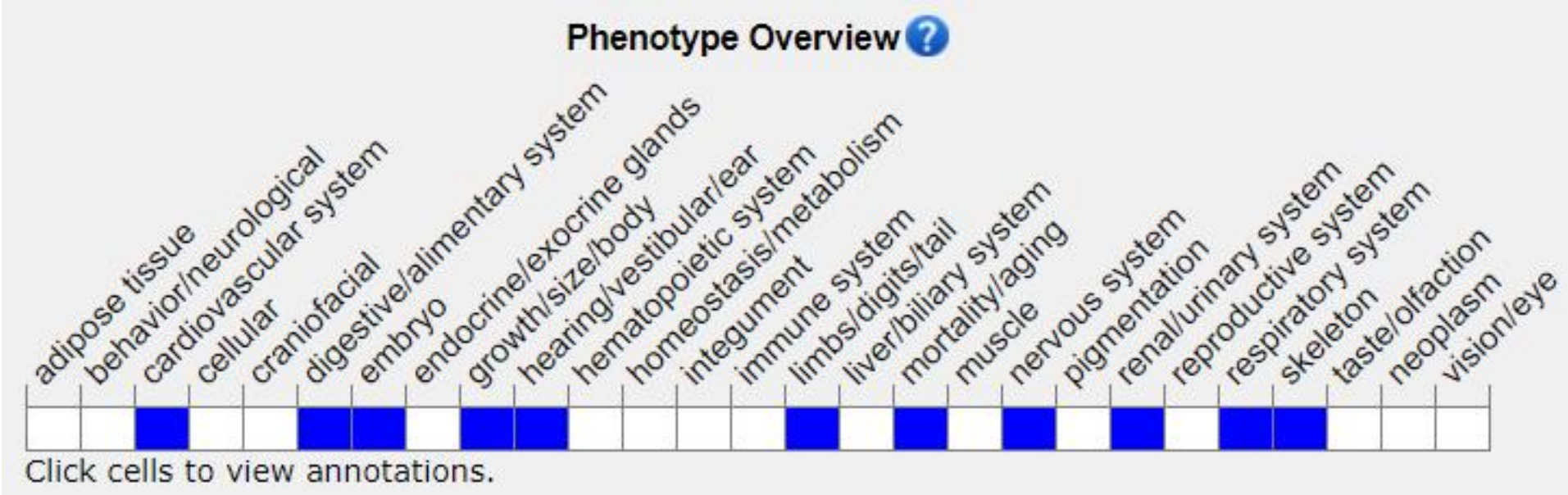
Source: http://asia.ensembl.org/

Protein Information



Source: https://www.ensembl.org

Mouse Phenotype Information (MGI)



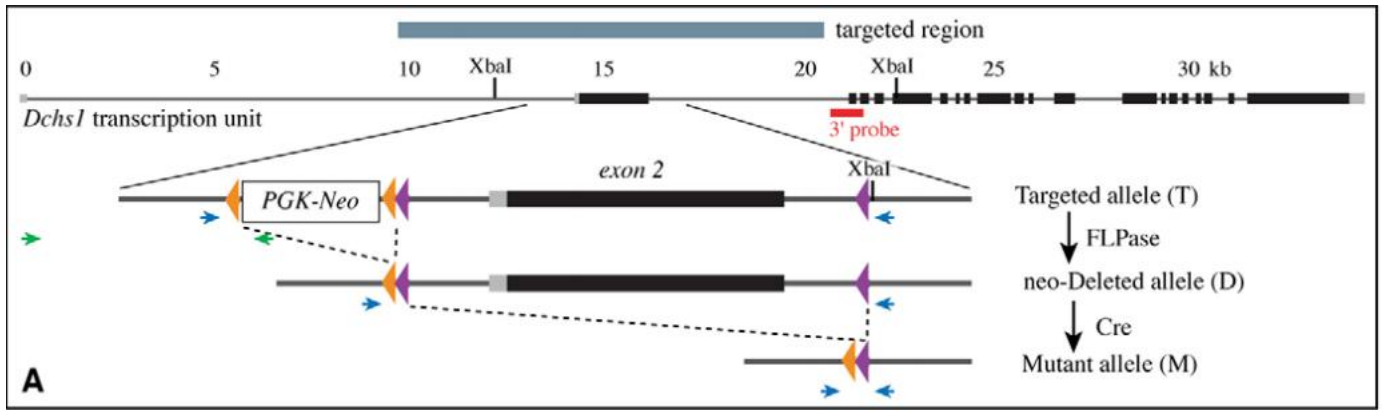
Mice homozygous for a knock-out allele exhibit postnatal lethality, growth retardation, small lungs, abnormal cochlea morphology, abnormal kidney morphology, cardiovascular abnormalities and skeletal abnormalities.

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

Important Information

- The knockout region overlaps with *Gm15645* gene, which may affect the function of this gene
- The knockout region contains start codon, translation may recognize new start codon and form new unknown protein.
- *Dchs1* is located on Chr 7. 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 risks of the mutation on gene transcription, RNA splicing and protein translation cannot be predicted at the existing technology level.

Reference



Dchs1 DNA was amplified from 129/SvImJ genomic DNA using Takara PrimeSTAR-HS polymerase in three parts: *Dchs1* exon2 plus partial introns (2936 bp), left arm (3997 bp) and right arm (3991 bp). These were cloned into pNZTK2 [a gift from R. Palmiter (University of Washington, Seattle)], where the *lacZ* gene was replaced by a PGK-Neo marker and adjacent loxP and FRT sites from p-loxP-2FRT-PGKneo (Transgenic Core, University of Michigan, MI, USA). Another loxP site was introduced by PCR. The loxP sites were 527 bp 5′ to exon 2, and 516 bp 3′ to exon 2.

[1] Mao Y, Mulvaney J, Zakaria S, Yu T, Morgan KM, Allen S, Basson MA, Francis-West P, Irvine KD. Characterization of a Dchs1 mutant mouse reveals requirements for Dchs1-Fat4 signaling during mammalian development. Development. 2011 Mar;138(5):947-57. doi: 10.1242/dev.057166. PMID: 21303848; PMCID: PMC3035097.