Dync2h1 Cas9-CKO Strategy

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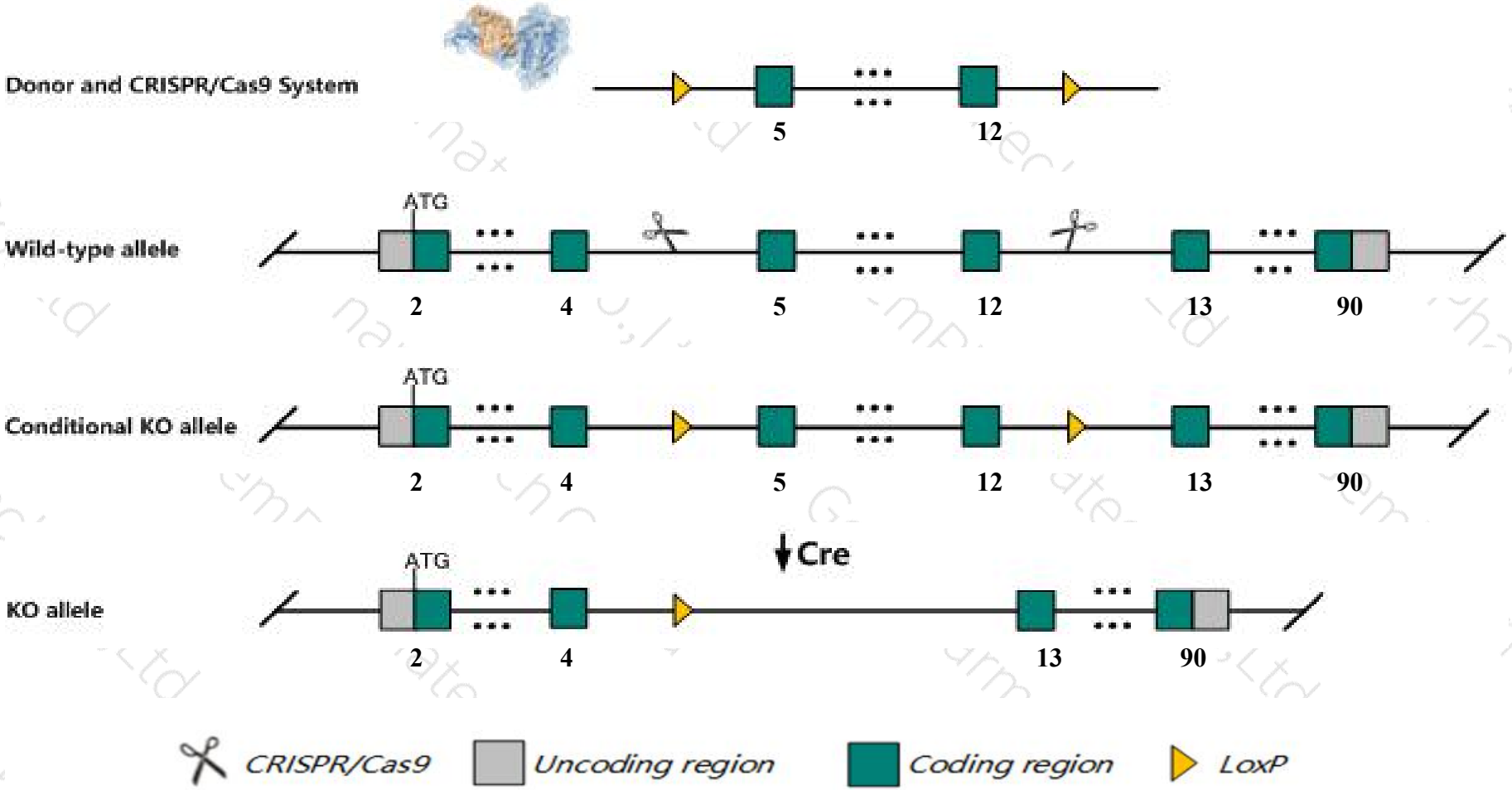
Project Overview

Project Name	***Dync2h1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Dync2h1* gene. The schematic diagram is as follows:



Technical routes

- The *Dync2h1* gene has 9 transcripts. According to the structure of *Dync2h1* gene, exon5-exon12 of *Dync2h1-204* (ENSMUST00000140466.7) transcript is recommended as the knockout region.The region contains 1159bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Dync2h1* 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,homozygotes for a gene trap allele show complete embryonic lethality with altered heart looping and brain morphology. chemically induced mutants show randomized heart looping and polydactyly. holoprosencephaly or exencephaly, dorsoventral forebrain patterning defects, micrognathia, and cardiac, renal, airway and eye defects may be observed.
- The *Dync2h1* gene is located on the Chr9. 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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Dync2h1 dynein cytoplasmic 2 heavy chain 1 [Mus musculus (house mouse)]

Gene ID: 110350, updated on 13-Mar-2020

Summary

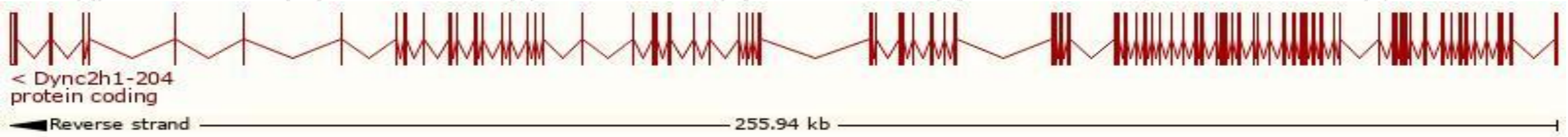
Official Symbol	Dync2h1 provided by MGI
Official Full Name	dynein cytoplasmic 2 heavy chain 1 provided by MGI
Primary source	MGI:MGI:107736
See related	Ensembl:ENSMUSG00000047193
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	4432416O06Rik, AI448217, D030010H02Rik, D330044F14Rik, DHC11, DHC1b, DHC2, Dnchc2, b2b414Clo, m152Asp, m407Asp, mDHC11
Expression	Broad expression in testis adult (RPKM 4.9), CNS E11.5 (RPKM 2.2) and 18 other tissuesSee more
Orthologs	human all

Transcript information（Ensembl）

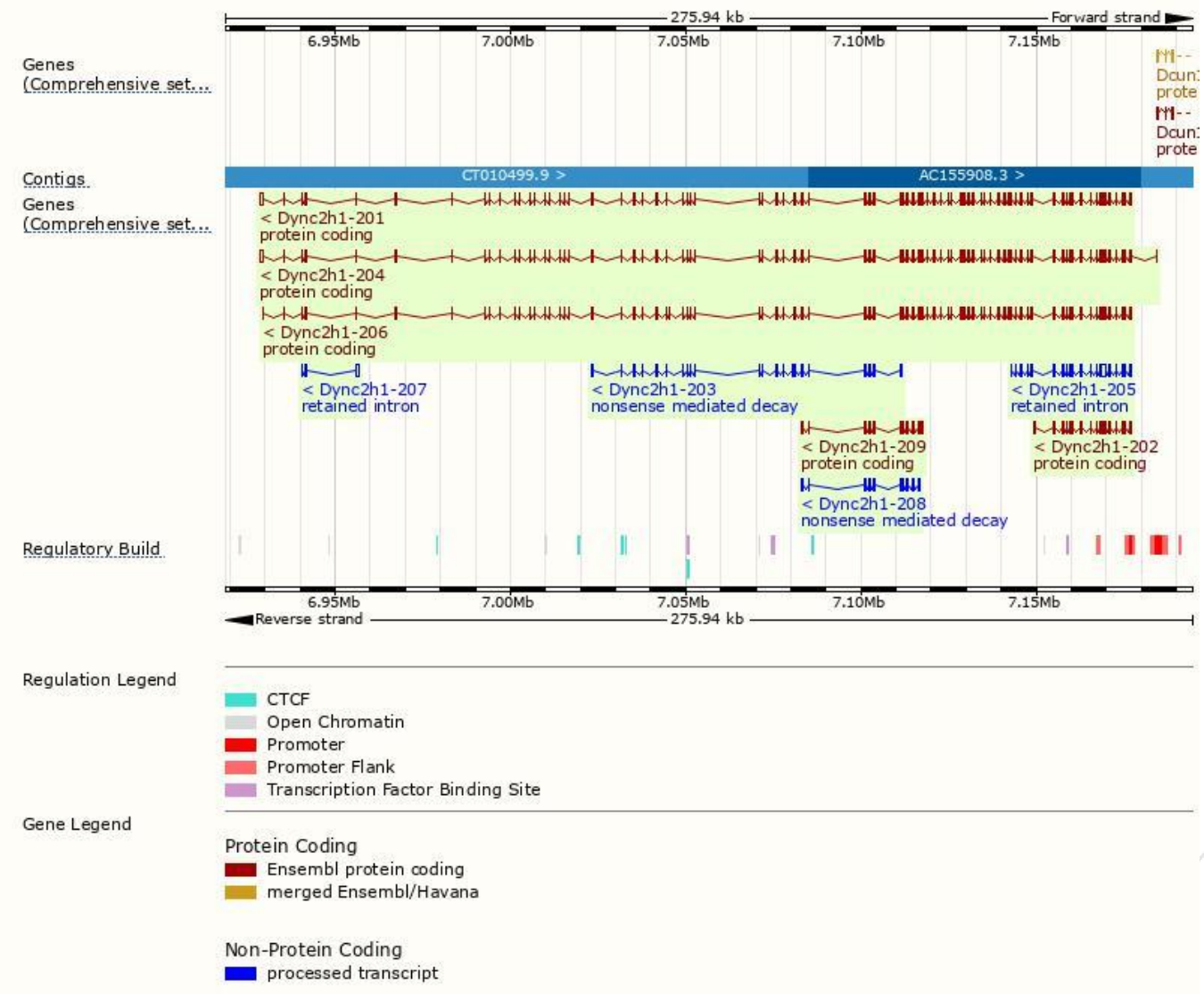
The gene has 9 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Dync2h1-204	ENSMUST00000140466.7	14264	4306aa	Protein coding	CCDS40528	Q45VK7	TSL:5 GENCODE basic APPRIS P2
Dync2h1-201	ENSMUST00000048417.12	13972	4306aa	Protein coding	CCDS40528	Q45VK7	TSL:1 GENCODE basic APPRIS P2
Dync2h1-206	ENSMUST00000147193.7	13103	4313aa	Protein coding	-	Q45VK7	TSL:5 GENCODE basic APPRIS ALT2
Dync2h1-202	ENSMUST00000139115.1	2892	916aa	Protein coding	-	D3Z025	TSL:1 GENCODE basic
Dync2h1-209	ENSMUST00000216097.1	1789	596aa	Protein coding	-	A0A1L1SS48	CDS 5' and 3' incomplete TSL:5
Dync2h1-203	ENSMUST00000139671.1	3335	385aa	Nonsense mediated decay	-	F6QLS2	CDS 5' incomplete TSL:1
Dync2h1-208	ENSMUST00000214191.1	1771	426aa	Nonsense mediated decay	-	A0A1L1SRI6	CDS 5' incomplete TSL:5
Dync2h1-205	ENSMUST00000147056.1	4365	No protein	Retained intron	-	-	TSL:2
Dync2h1-207	ENSMUST00000152934.1	933	No protein	Retained intron	-	-	TSL:5

The strategy is based on the design of *Dync2h1-204* transcript,the transcription is shown below:

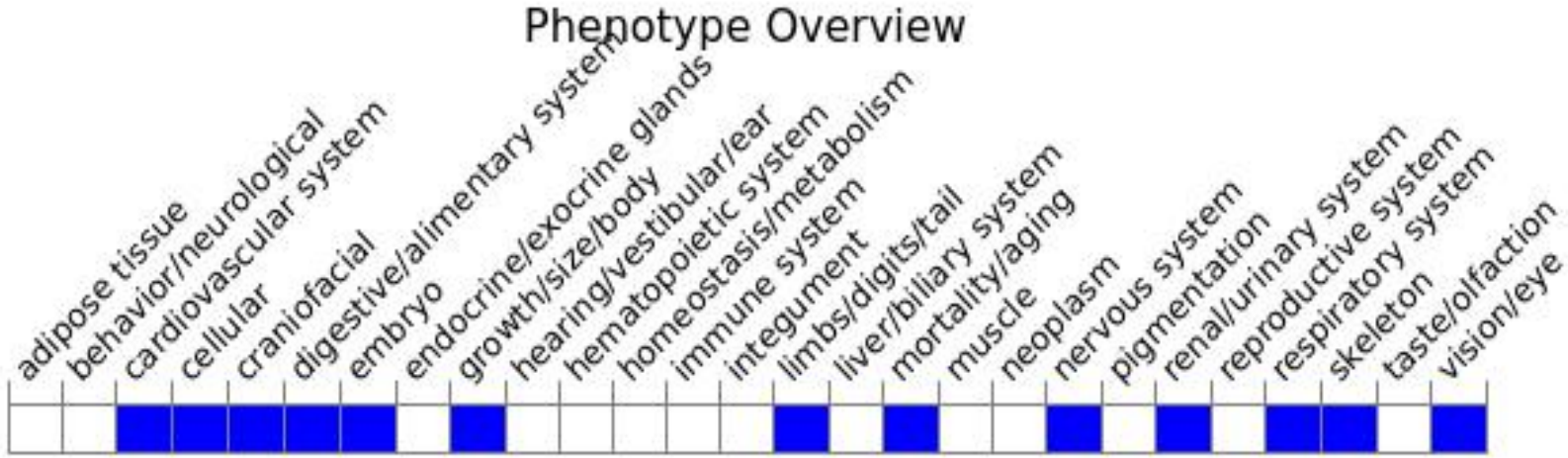


Genomic location distribution



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,homozygotes for a gene trap allele show complete embryonic lethality with altered heart looping and brain morphology. Chemically induced mutants show randomized heart looping and polydactyly. Holoprosencephaly or exencephaly, dorsoventral forebrain patterning defects, micrognathia, and cardiac, renal, airway and ey defects may be observed.

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

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