GemPharmatech™

Sdhc Cas9-CKO Strategy

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Overview

Target Gene Name

- Sdhc

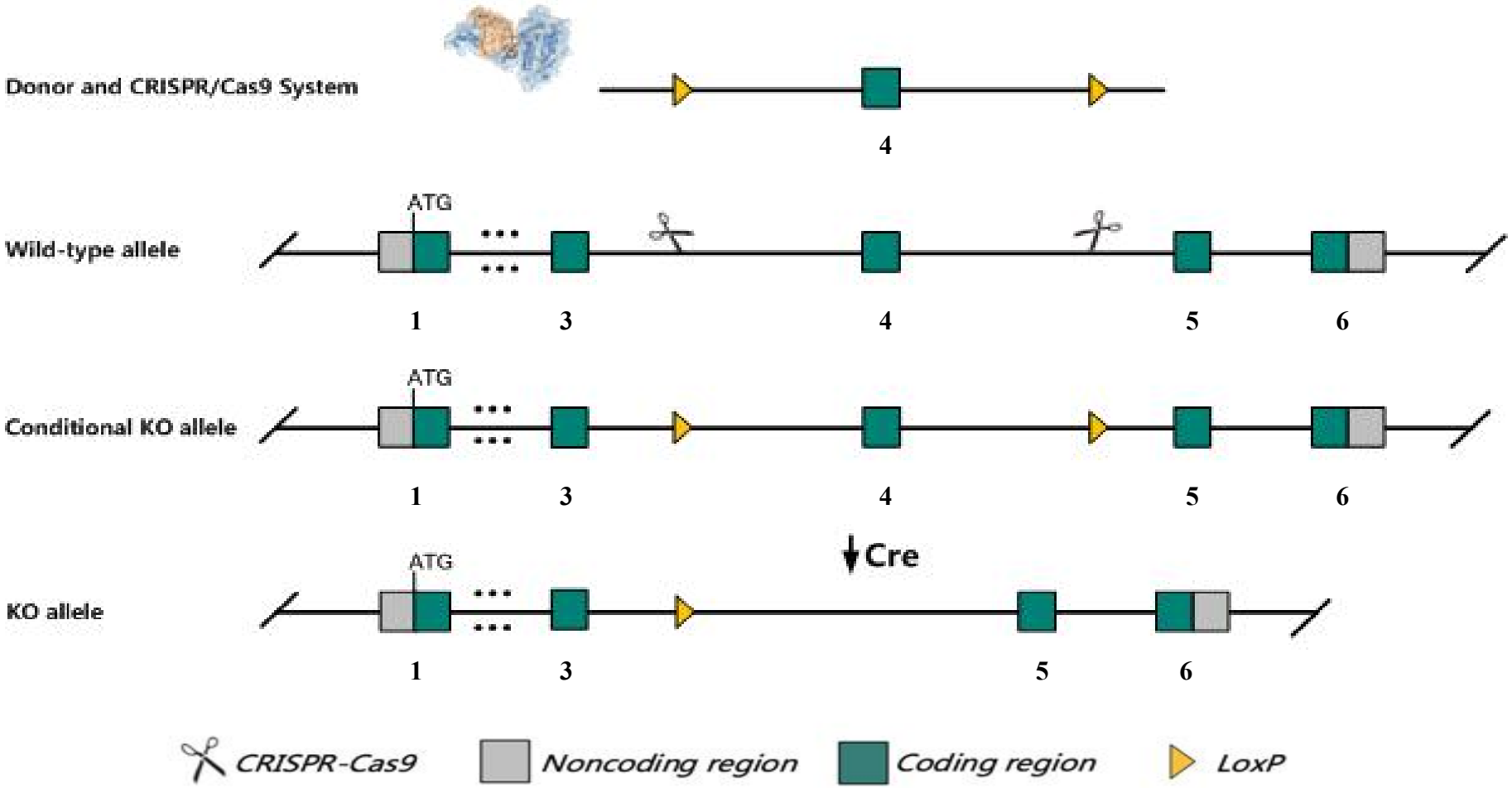
Project Type

- Cas9-CKO

Genetic Background

- C57BL/6JGpt

Strain Strategy



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

Technical Information

- The *Sdhc* gene has 3 transcripts. According to the structure of *Sdhc* gene, exon4 of *Sdhc*-202 (ENSMUST00000111336.10) transcript is recommended as the knockout region. The region contains 62bp coding sequence. Knocking out the region will result in disruption of protein function.
- In this project we use CRISPR-Cas9 technology to modify *Sdhc* 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

Sdhc succinate dehydrogenase complex, subunit C, integral membrane protein [Mus musculus (house mouse)]

Gene ID: 66052, updated on 12-Apr-2023

Summary

Official Symbol	Sdhc provided by MGI
Official Full Name	succinate dehydrogenase complex, subunit C, integral membrane protein provided byMGI
Primary source	MGI:MGI:1913302
See related	Ensembl:ENSMUSG00000058076
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	0610010E03Rik
Summary	Predicted to enable electron transfer activity; metal ion binding activity; and succinate dehydrogenase activity. Predicted to be involved in mitochondrial electron transport, succinate to ubiquinone. Predicted to act upstream of or within tricarboxylic acid cycle. Located in mitochondrion. Is expressed in several structures, including alimentary system; brain; cardiovascular system; genitourinary system; and sensory organ. Used to study Leigh disease. Human ortholog(s) of this gene implicated in Carney-Stratakis syndrome; gastrointestinal stromal tumor; lung non-small cell carcinoma; and paraganglioma. Orthologous to human SDHC (succinate dehydrogenase complex subunit C). [provided by Alliance of Genome Resources, Apr 2022]
Expression	Ubiquitous expression in heart adult (RPKM 368.5), kidney adult (RPKM 283.2) and 28 other tissuesSee more
Orthologs	human all

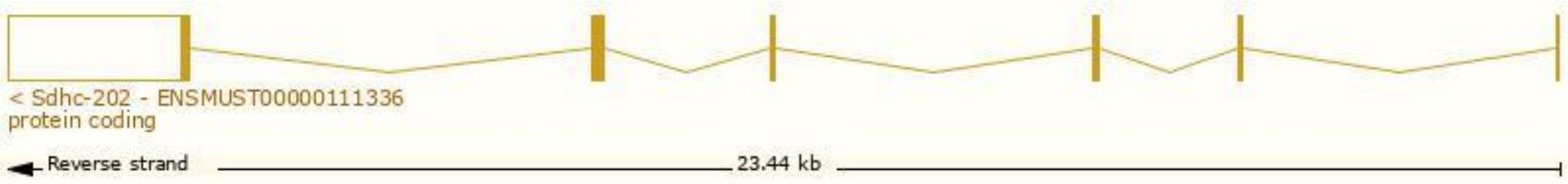
Source: https://www.ncbi.nlm.nih.gov/

Transcript Information

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

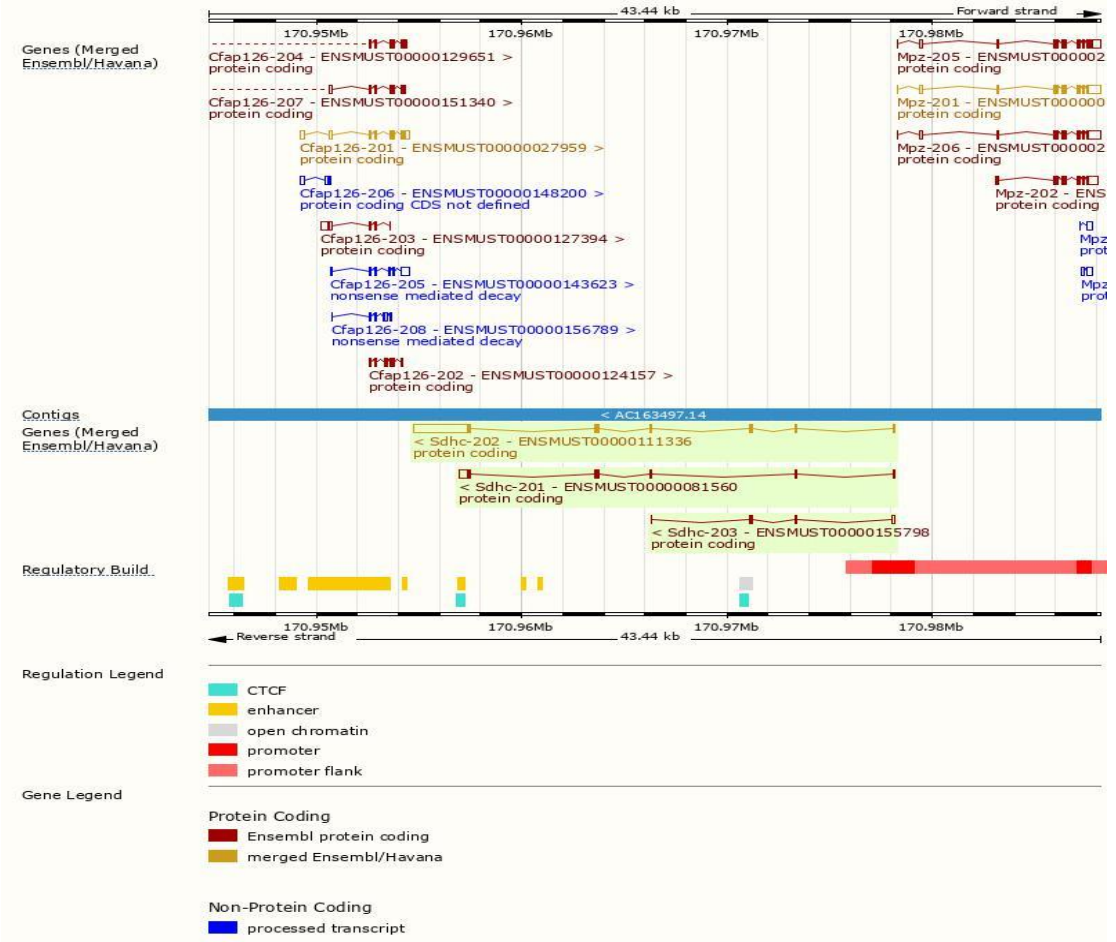
Transcript ID	Name	bp	Protein	Biotype	CCDS	UniProt Match	Flags
ENSMUST00000111336.10	Sdhc-202	3171	169aa	Protein coding	CCDS35772	Q9CZB0	Ensembl Canonical, GENCODE basic, APPRIS P1, TSL:1
ENSMUST00000081560.5	Sdhc-201	815	135aa	Protein coding		F8WGB3	GENCODE basic, TSL:3
ENSMUST00000155798.2	Sdhc-203	298	32aa	Protein coding		D3Z1A8	TSL:5, CDS 3' incomplete

The strategy is based on the design of *Sdhc*-202 transcript, the transcription is shown below:



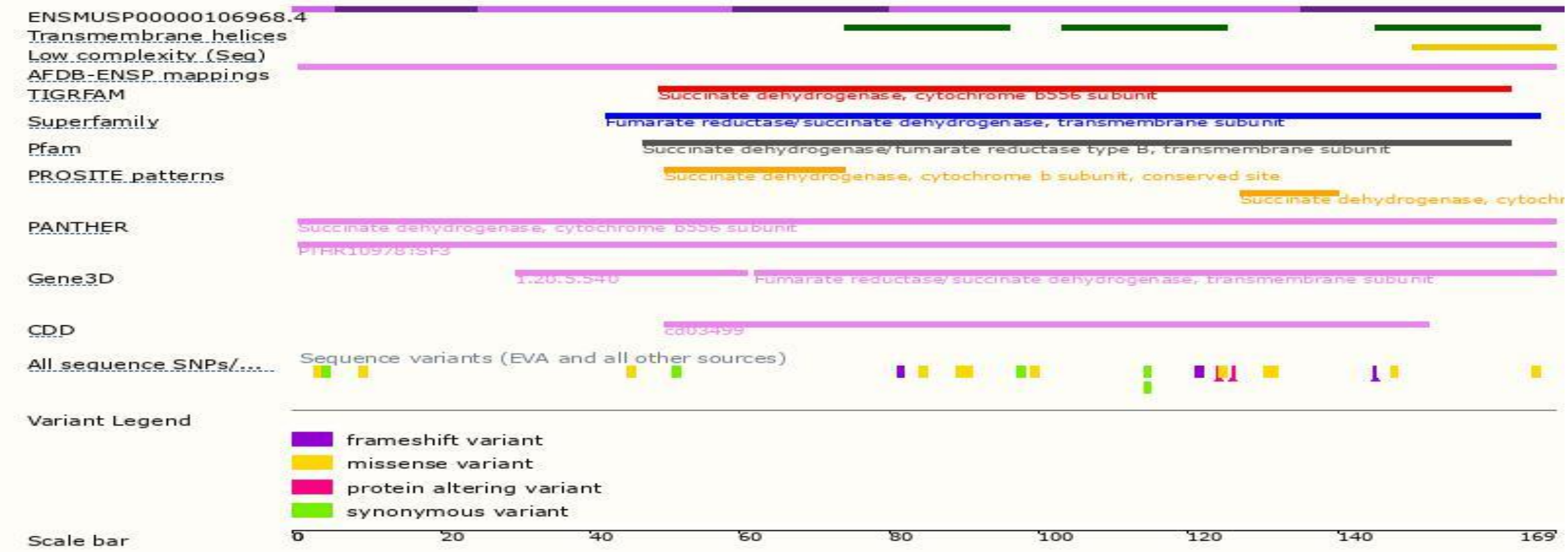
Source: https://www.ensembl.org

Genomic Information



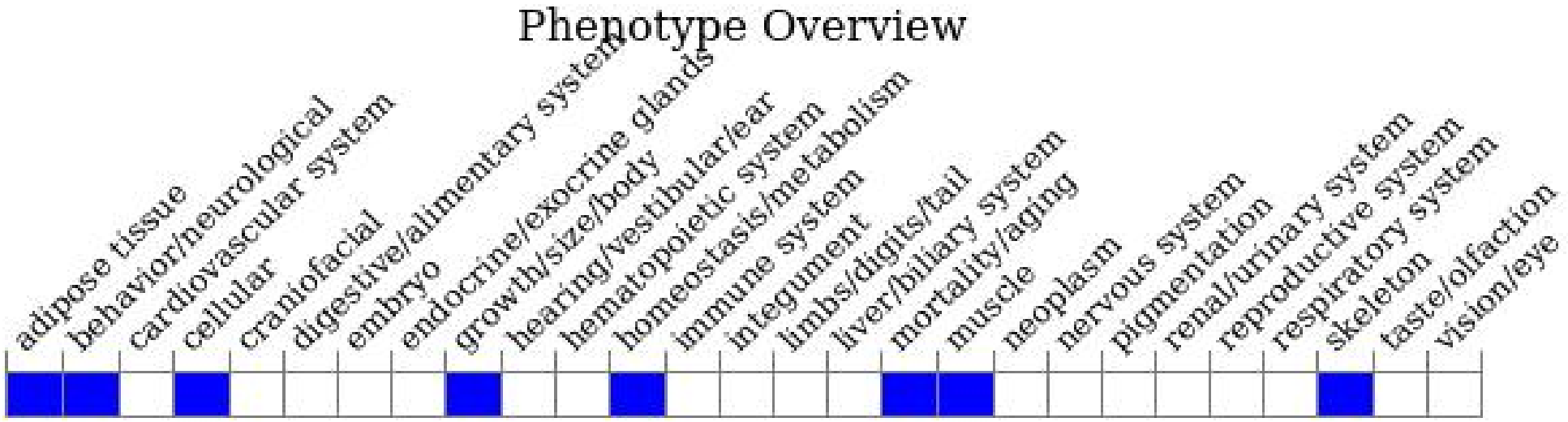
Source: : https://www.ensembl.org

Protein Information



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

Mouse Phenotype Information (MGI)



- Heterozygous compound knockouts (with Sdhb or Sdhb and Sdhd) show reduced increase in blood hemoglobin under hypoxic conditions.

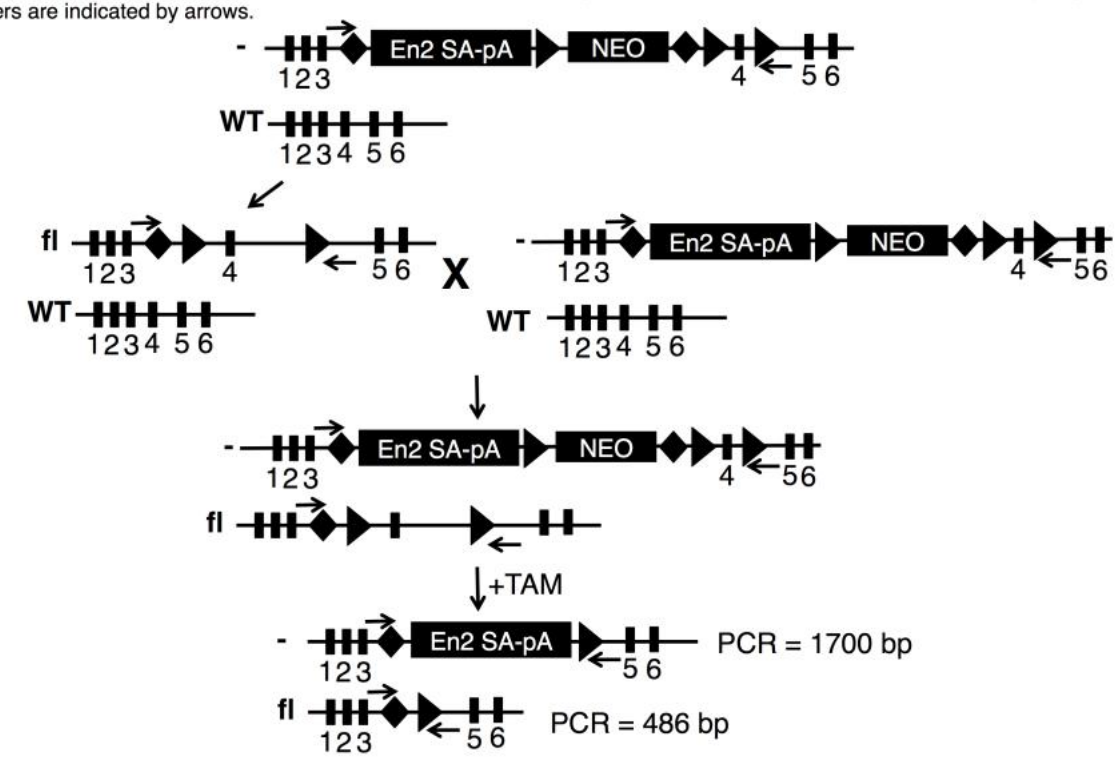
Source: https://www.informatics.jax.org

Important Information

- According to the MGI information,heterozygous compound knockouts (with Sdhb or Sdhb and Sdhd) show reduced increase in blood hemoglobin under hypoxic conditions.Mice homozygous for a knock-out allele exhibit embryonic lethality prior to tooth bud stage.
- The effect of transcript-203 is unknwon.
- *Sdhc* is located on Chr1. 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.

Reference

Supplemental Figure. 2. Generation of *Sdhc* conditional knockout mice. Founder mice have a wild type (WT) SDHC allele and an *Sdhc* gene trap allele (-) in which an *Engrailed* polyadenylation site (En2 SA) terminates transcription creating a truncated mRNA. The *Sdhc* floxed allele (fl) mice wascreated by FLP recombination between *FRT* sites (diamonds) in a prior breeding, yielding loxP recombination sites flanking *Sdhc* exon 4 in the fl allele. Mating between *Sdhc* (-/WT) and *Sdhc* (fl/WT) mice yielded *Sdhc* (-/fl) mice. Breeding onto a CRE^{ER}-TM background allows disruption of both *Sdhc* fl alleles by recombination between loxP sites (triangles) upon Tamoxifen (TAM) treatment. Genotyping primers are indicated by arrows.



Her YF, et al., Oxygen concentration controls epigenetic effects in models of familial paraganglioma. PLoS One. 2015;10(5):e0127471