Scn8a Cas9-KO Strategy

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Design Date: **2019-11-22**

Project Overview

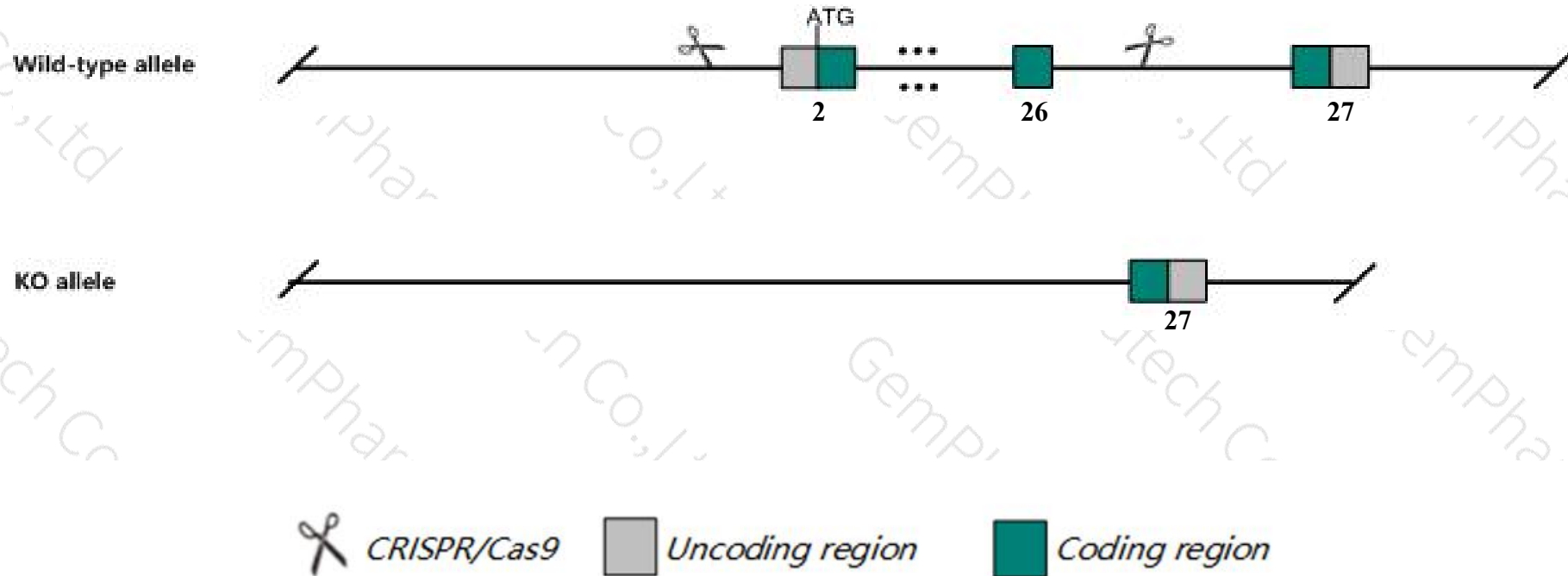|	
Project Name	*Scn8a*
Project type	**Cas9-KO**
Strain background	**C57BL/6JGpt**

Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Scn8a* gene. The schematic diagram is as follows:

➢ The *Scn8a* gene has 20 transcripts. According to the structure of *Scn8a* gene, exon2-exon26 of *Scn8a-201*

(ENSMUST00000082209.12) transcript is recommended as the knockout region.The region contains start codon ATG.

Knock out the region will result in disruption of protein function.

➢ In this project we use CRISPR/Cas9 technology to modify *Scn8a* gene. The brief process is as follows: CRISPR/Cas9 system

Notice

➢ According to the existing MGI data,Spontaneous mutant homozygotes have ataxia, dystonia, muscular atrophy, progressive paralysis, Purkinje cell loss, in some cases severe head-tossing and for severe alleles, juvenile lethality. A mild, semidominant ENU allele causes deafness of variable penetrance and severity and mild tremor.

➢ The *Scn8a* gene is located on the Chr15. 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）

Scn8a sodium channel, voltage-gated, type VIII, alpha [Mus musculus (house mouse)]
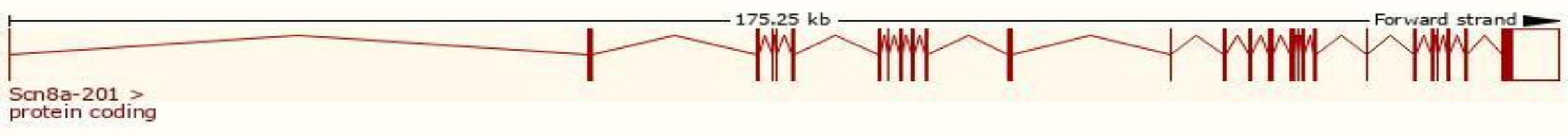
Gene ID: 20273, updated on 19-Feb-2019

▲ Summary

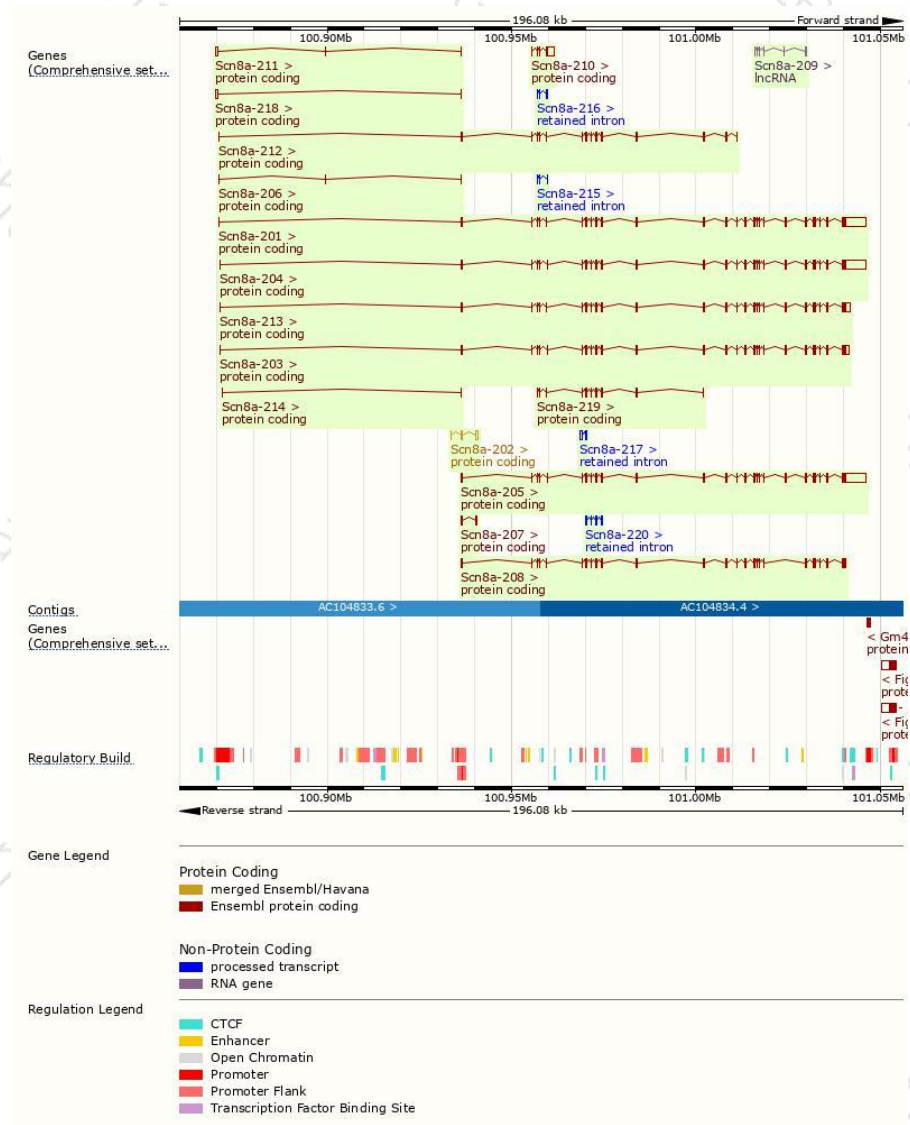|	
Official Symbol	Scn8a provided by MGI
Official Full Name	sodium channel, voltage-gated, type VIII, alpha provided by MGI
Primary source	MGI:MGI:103169
See related	Ensembl:ENSMUSG00000023033
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	AI853486, C630029C19Rik, NaCh6, Nav1.6, dmu, med, mnd-2, mnd2, nmf2, nmf335, nmf58, nur14, seal
Expression	Biased expression in cortex adult (RPKM 21.8), cerebellum adult (RPKM 21.1) and 5 other tissues See more
Orthologs	human all

Transcript information（Ensembl）

The gene has 20 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Scn8a-201	ENSMUST00000082209.12	11293	1978aa	Protein coding	CCDS57010	F6U329	TSL:5 GENCODE basic APPRIS P5
Scn8a-205	ENSMUST00000108910.9	11232	1978aa	Protein coding	CCDS57011	F7D6K4	TSL:1 GENCODE basic APPRIS ALT1
Scn8a-213	ENSMUST00000201549.3	7120	1978aa	Protein coding	CCDS57010	F6U329	TSL:5 GENCODE basic APPRIS P5
Scn8a-203	ENSMUST00000108908.5	7030	1978aa	Protein coding	CCDS57011	F7D6K4	TSL:5 GENCODE basic APPRIS ALT1
Scn8a-204	ENSMUST00000108909.8	11436	1988aa	Protein coding	-	F7D6J5	TSL:5 GENCODE basic
Scn8a-208	ENSMUST00000200963.3	5814	1937aa	Protein coding	-	A0A0J9YUW5	TSL:5 GENCODE basic
Scn8a-212	ENSMUST00000201518.3	2565	804aa	Protein coding	-	A0A0J9YTW4	CDS 3' incomplete TSL:1
Scn8a-210	ENSMUST00000201438.3	2110	132aa	Protein coding	-	A0A0J9YUL0	CDS 5' incomplete TSL:3
Scn8a-219	ENSMUST00000202702.1	1618	539aa	Protein coding	-	A0A0J9YTW2	5' and 3' truncations in transcript evidence prevent annotation of the start and the end of the CDS. CDS 5' and 3' incomplete TSL:5
Scn8a-202	ENSMUST00000096198.9	1072	102aa	Protein coding	-	Q4KL32	TSL:1 GENCODE basic
Scn8a-211	ENSMUST00000201484.3	683	1aa	Protein coding	-	-	CDS 3' incomplete TSL:1
Scn8a-207	ENSMUST00000200959.1	587	100aa	Protein coding	-	A0A0J9YUK3	TSL:3 GENCODE basic
Scn8a-218	ENSMUST00000202527.3	533	1aa	Protein coding	-	-	CDS 3' incomplete TSL:1
Scn8a-214	ENSMUST00000202071.1	322	1aa	Protein coding	-	-	CDS 3' incomplete TSL:1
Scn8a-206	ENSMUST00000200933.3	290	1aa	Protein coding	-	-	CDS 3' incomplete TSL:1
Scn8a-220	ENSMUST00000202971.1	840	No protein	Retained intron	-	-	TSL:2
Scn8a-217	ENSMUST00000202452.1	681	No protein	Retained intron	-	-	TSL:3
Scn8a-216	ENSMUST00000202349.3	514	No protein	Retained intron	-	-	TSL:2
Scn8a-215	ENSMUST00000202347.1	326	No protein	Retained intron	-	-	TSL:5
Scn8a-209	ENSMUST00000201246.1	903	No protein	lncRNA	-	-	TSL:5

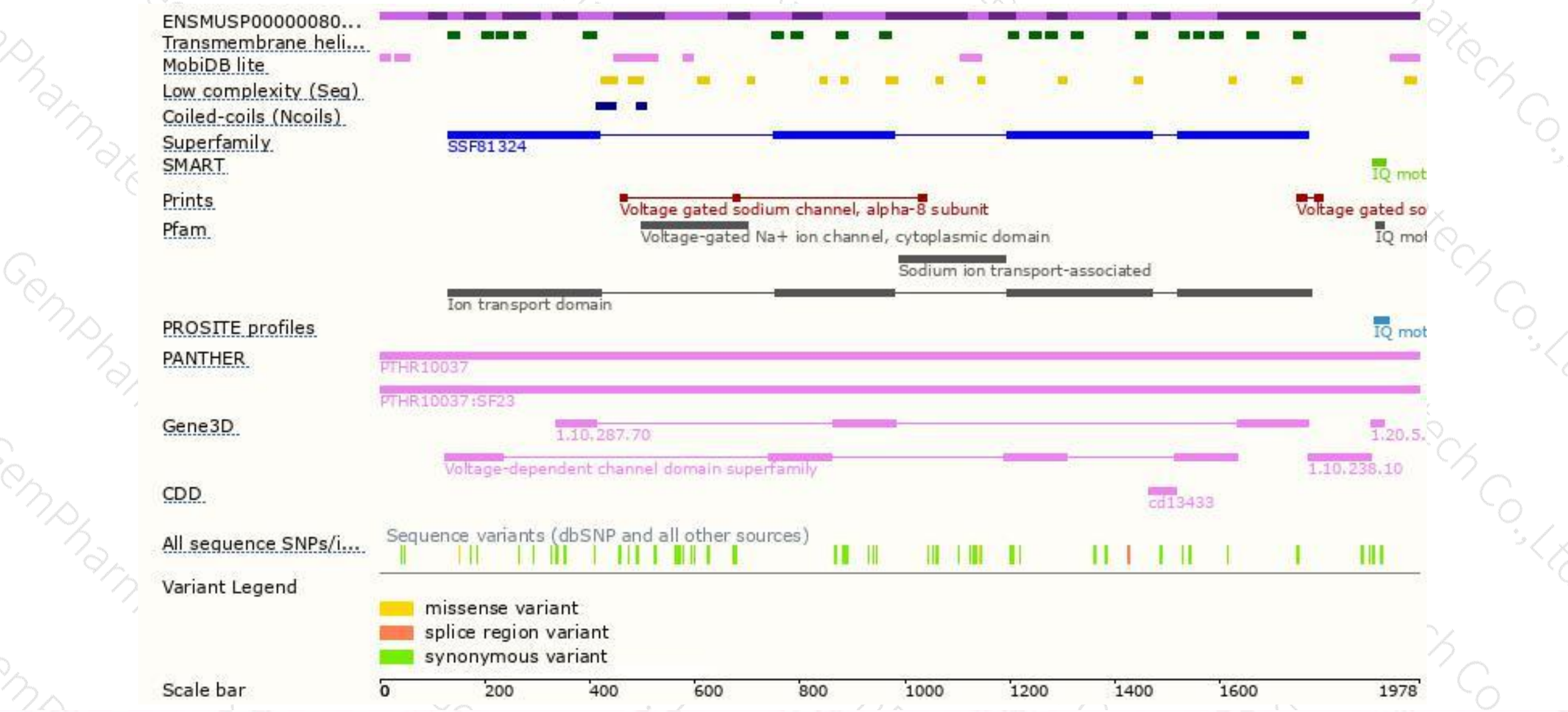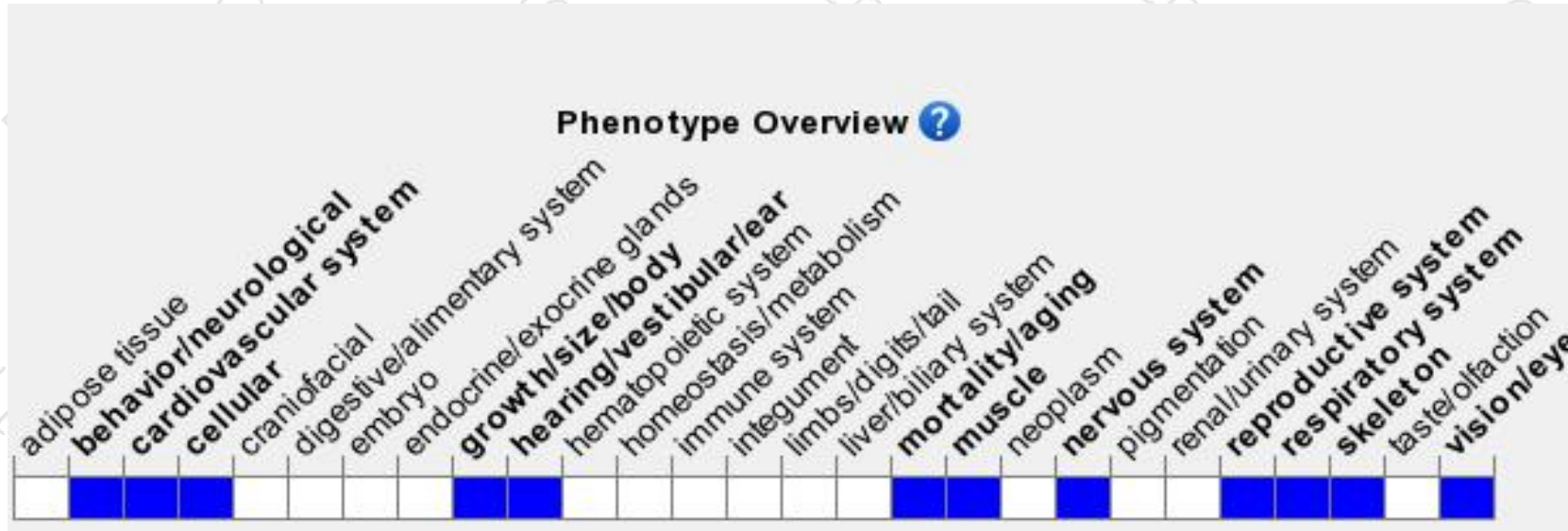The strategy is based on the design of *Scn8a-201* transcript,The transcription is shown below

Genomic location distribution

Protein domain

ENSMUSP00000080...											
Transmembrane heli...											
MobiDB lite											
Low complexity (Seg)											
Coiled-coils (Ncoils)											
Superfamily	SSF81324										
SMART											IQ mot
Prints			Voltage gated sodium channel, alpha-8 subunit								Voltage gated so
Pfam			Voltage-gated Na+ ion channel, cytoplasmic domain								IQ mot
						Sodium ion transport-associated					
		Ion transport domain									
PROSITE profiles											IQ mot
PANTHER	PTHR10037										
	PTHR10037:SF23										
Gene3D			1.10.287.70								1.20.5.
		Voltage-dependent channel domain superfamily									1.10.238.10
CDD									cd13433		
All sequence SNPs/i...	Sequence variants (dbSNP and all other sources)										

Variant Legend

- 🟨 missense variant
- 🟧 splice region variant
- 🟩 synonymous variant

Scale bar 0   200   400   600   800   1000   1200   1400   1600   1978

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,Spontaneous mutant homozygotes have ataxia, dystonia, muscular atrophy, progressive paralysis, Purkinje cell loss, in some cases severe head-tossing and for severe alleles, juvenile lethality. A mild, semidominant ENU allele causes deafness of variable penetrance and severity and mild tremor.

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