Txnrd1 Cas9-CKO *Strategy*

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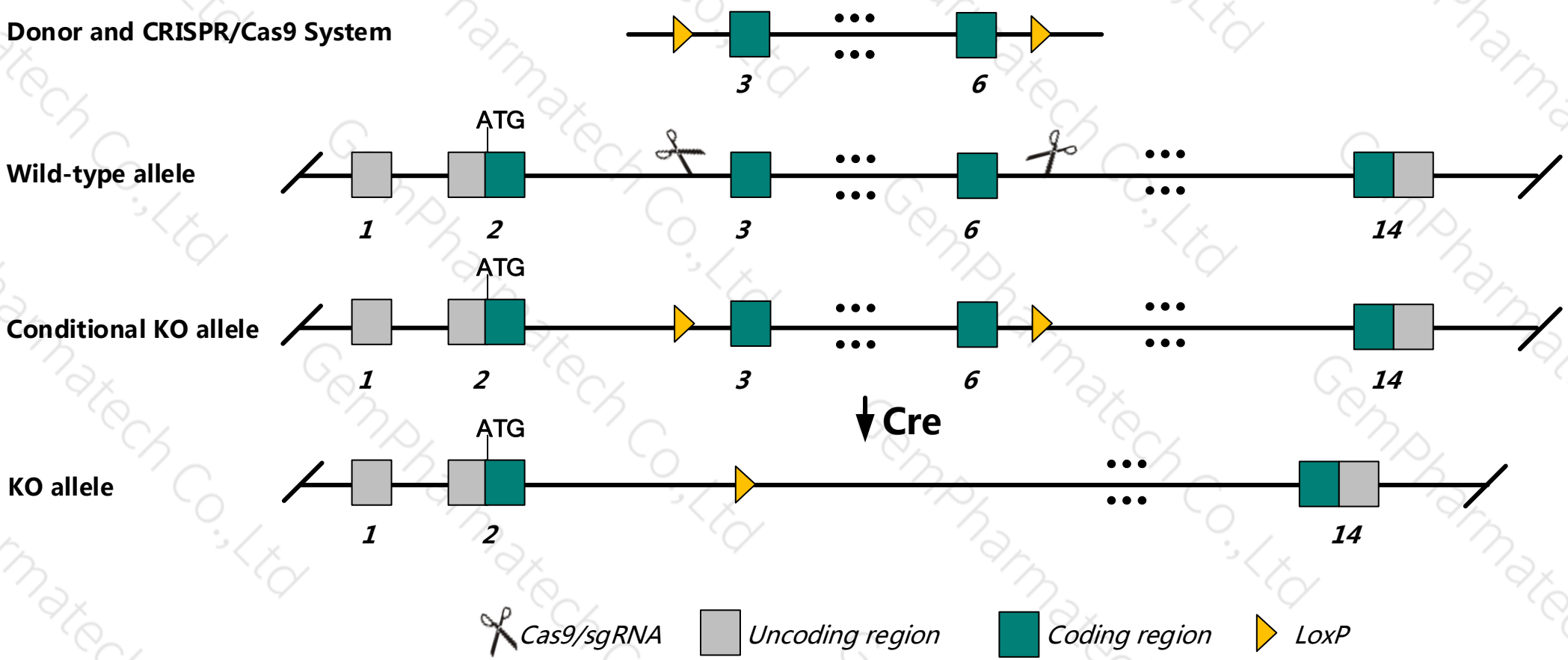
Project Overview

Project Name	***Txnrd1***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Txnrd1* gene. The schematic diagram is as follows:



Technical routes

- The *Txnrd1* gene has 8 transcripts.According to the structure of *Txnrd1* gene, exon3-exon6 of *Txnrd1*-206 (ENSMUST00000219442.1) transcript is recommended as the knockout region.The region contains 452bp coding sequence.Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Txnrd1* gene. The brief process is as follows: sgRNA was transcribed in vitro, donor vector was constructed.Cas9, sgRNA 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 was knocked out after mating with mice expressing Cre recombinase, resulting in the loss of function of the target gene in specific tissues or cell types.

Notice

- According to the existing MGI data，Homozygous null mice exhibit early embryonic lethality (by E10.5) and display severe growth retardation and fail to turn. Embryos also exhibit decreased cell proliferation.
- The *Txnrd1* gene is located on the Chr10. 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 loxp insertion on gene transcription, RNA splicing and protein translation cannot be predicted at the existing technology level.

Gene information （NCBI）

Txnrd1 thioredoxin reductase 1 [*Mus musculus* (house mouse)]

Gene ID: 50493, updated on 12-May-2019

Summary

Official Symbol	Txnrd1 provided by MGI
Official Full Name	thioredoxin reductase 1 provided by MGI
Primary source	MGI:MGI:1354175
See related	Ensembl:ENSMUSG00000020250
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	TR; TR1; TrxR1
Summary	The protein encoded by this gene belongs to the pyridine nucleotide-disulfide oxidoreductase family, and is a member of the thioredoxin (Trx) system. Three thioredoxin reductase (TrxR) isozymes are found in mammals. TrxRs are selenocysteine-containing flavoenzymes, which reduce thioredoxins, as well as other substrates, and play a key role in redox homoeostasis. This gene encodes an ubiquitously expressed, cytosolic form of TrxR, which functions as a homodimer containing FAD, and selenocysteine (Sec) at the active site. Sec is encoded by UGA codon that normally signals translation termination. The 3' UTRs of selenoprotein mRNAs contain a conserved stem-loop structure, the Sec insertion sequence (SECIS) element, which is necessary for the recognition of UGA as a Sec codon rather than as a stop signal. Alternative splicing, primarily at the 5' end, results in transcript variants encoding same or different isoforms. [provided by RefSeq, May 2017]
Expression	Ubiquitous expression in duodenum adult (RPKM 37.4), large intestine adult (RPKM 32.2) and 28 other tissues See more
Orthologs	human all

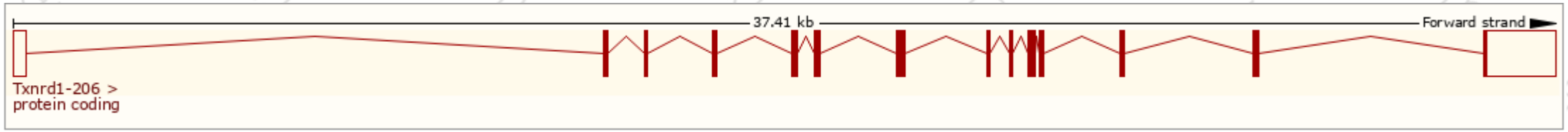
Transcript information（ Ensembl ）

The gene has 8 transcripts, and all transcripts are shown below:

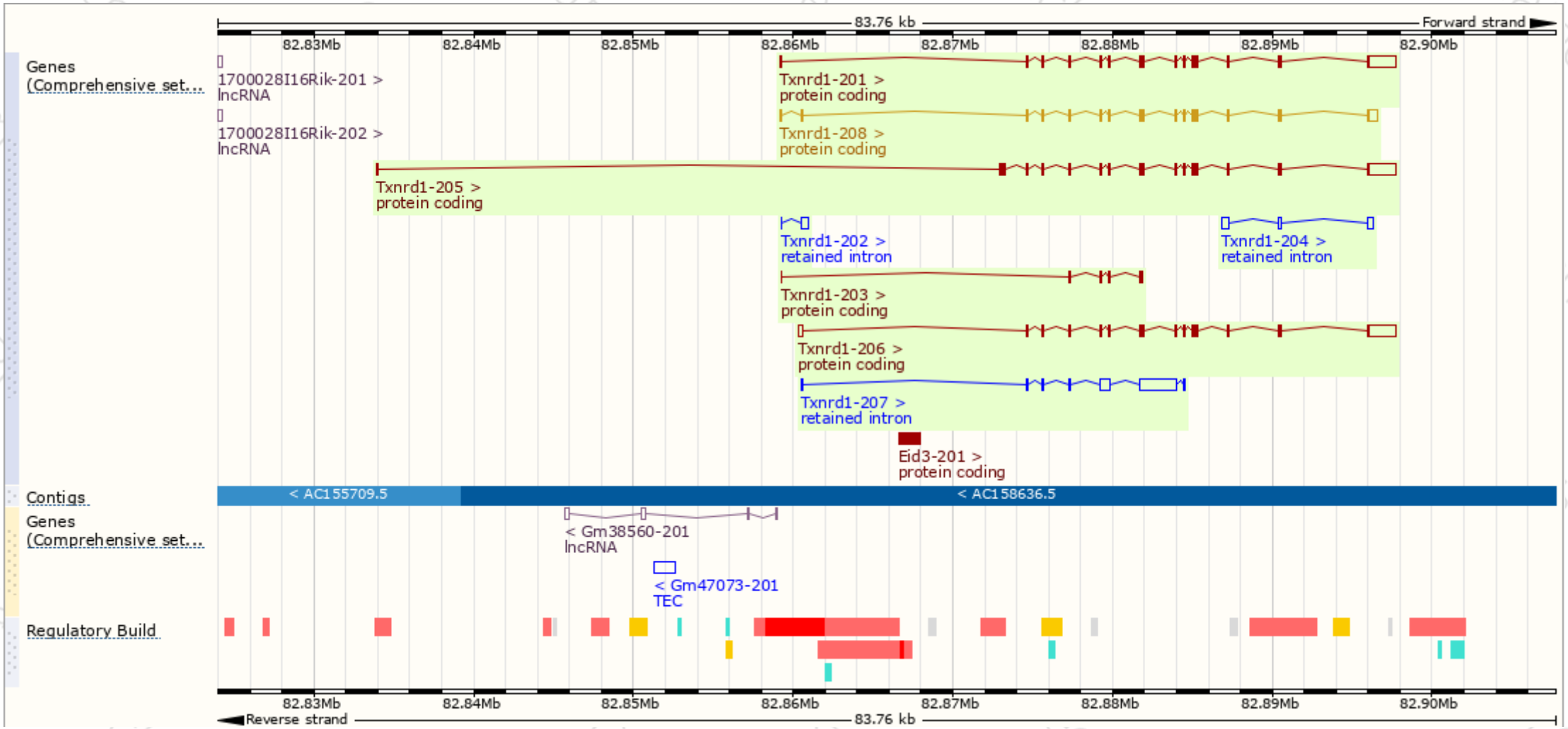
Show/hide columns (1 hidden) Filter

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Txnrd1-206	ENSMUST00000219442.1	3531	499aa	Protein coding	CCDS24072	Q9JMH6	TSL:5 GENCODE basic APPRIS P1
Txnrd1-201	ENSMUST00000020484.7	3325	499aa	Protein coding	CCDS24072	Q9JMH6	TSL:1 GENCODE basic APPRIS P1
Txnrd1-208	ENSMUST00000219962.1	2297	499aa	Protein coding	CCDS24072	Q9JMH6	TSL:1 GENCODE basic APPRIS P1
Txnrd1-205	ENSMUST00000219368.1	3622	613aa	Protein coding	-	Q9JMH6	TSL:1 GENCODE basic
Txnrd1-203	ENSMUST00000218694.1	581	164aa	Protein coding	-	A0A1W2P6U1	CDS 3' incomplete TSL:3
Txnrd1-207	ENSMUST00000219911.1	3449	No protein	Retained intron	-	-	TSL:5
Txnrd1-204	ENSMUST00000218724.1	894	No protein	Retained intron	-	-	TSL:1
Txnrd1-202	ENSMUST00000218082.1	483	No protein	Retained intron	-	-	TSL:1

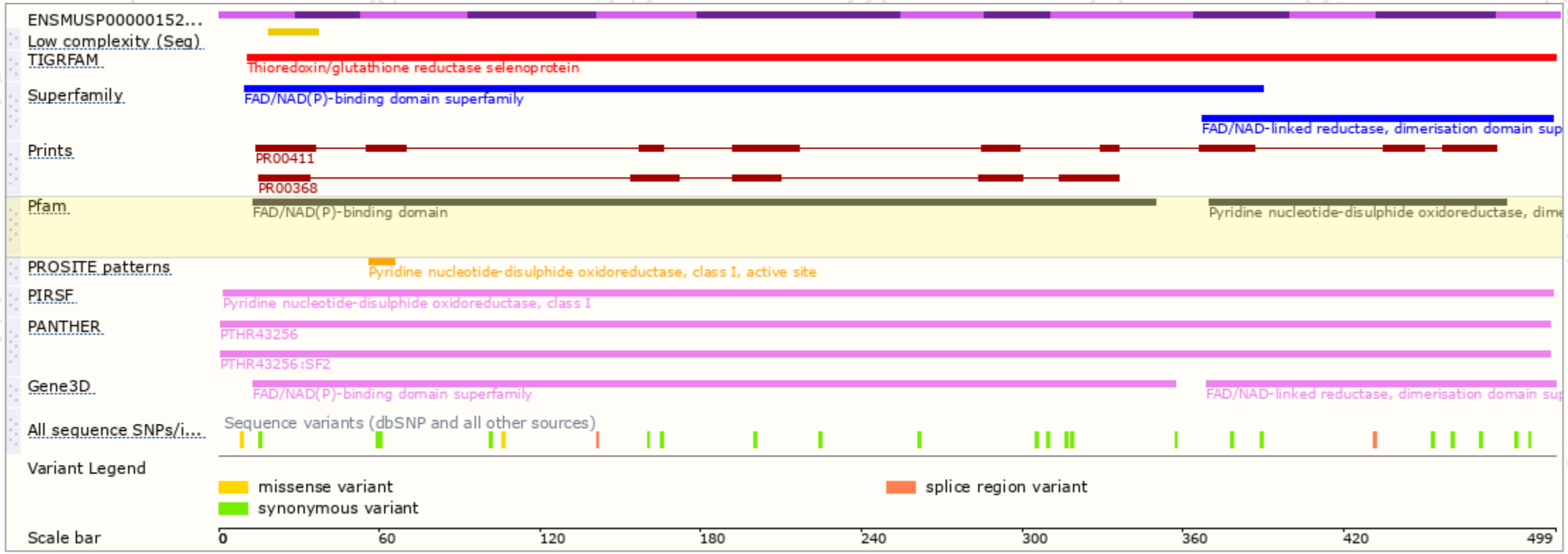
The strategy is based on the design of *Txnrd1*-206 transcript,The transcription is shown below



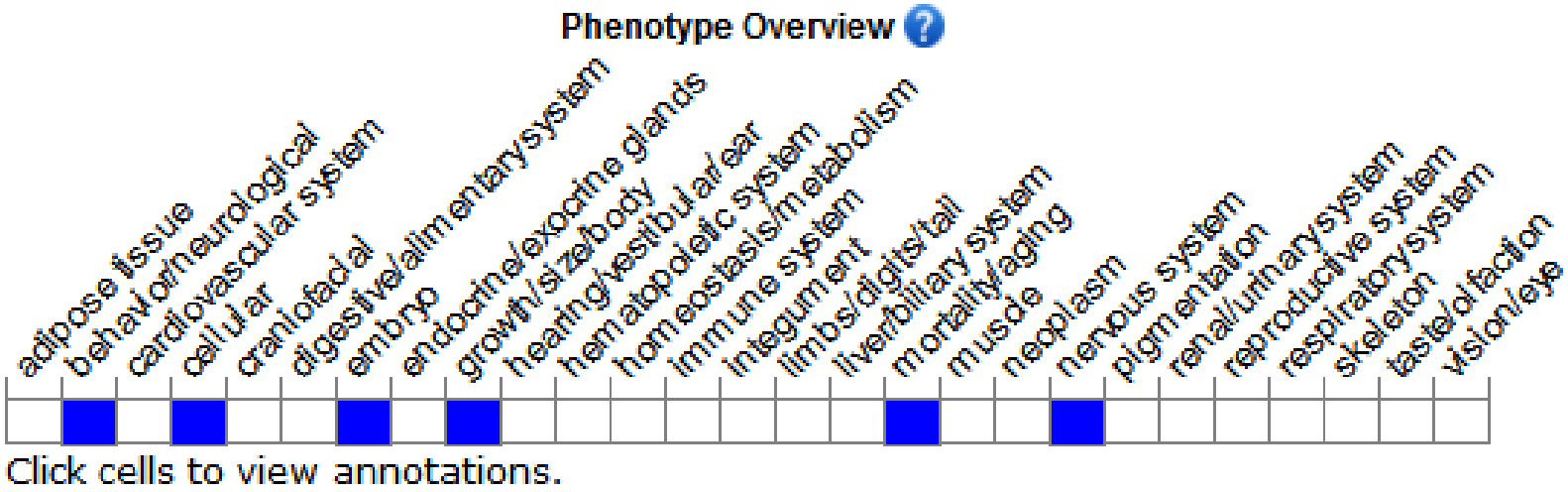
Genomic location distribution



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,Homozygous null mice exhibit early embryonic lethality (by E10.5) and display severe growth retardation and fail to turn. Embryos also exhibit decreased cell proliferation.

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

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