Obsl1-p.A1202V cas9-ki(PM) Mouse Model Strategy

-CRISPR/Cas9 technology

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Reviewer: Yanhua Shen

Design Date: 2021-8-23

Project Overview

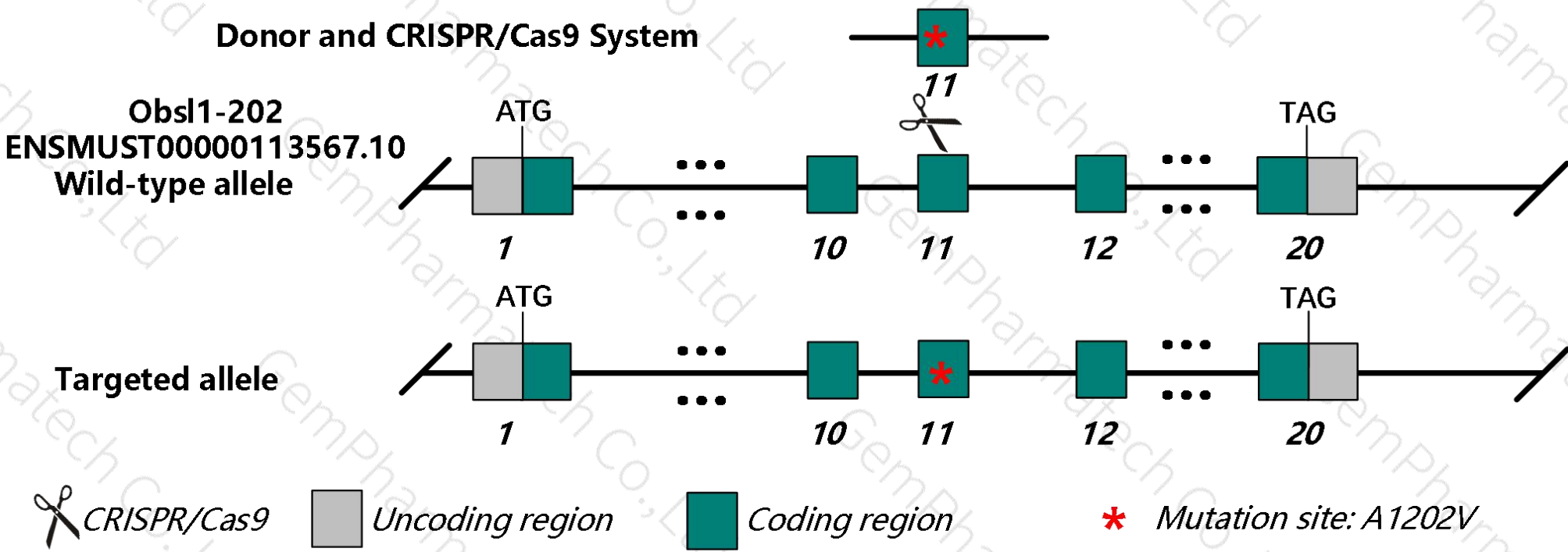|	
Project Name	**Obsl1-p.A1202V**
Project type	**cas9-ki(PM)**
Strain background	**C57BL/6JGpt**

Strategy

This model uses CRISPR/Cas9 technology to edit the *Obsl1* gene and the schematic diagram is as follow:

Technical Description

- The mouse *Obsl1* gene has 8 transcripts.The human *OBSL1* gene has 32 transcripts.

- According to the structure of *Obsl1* gene and requirements of customer, the 1202th amino acid(A) of human *OBSL1* gene(NM_015311.3) corresponds to the 1202th amino acid(A) of mouse *Obsl1* gene after comparing homology of mouse *Obsl1* gene and human *OBSL1* gene.This project produced *Obsl1*-A1202V point mutation on exon11 of the transcript of *Obsl1*-202(ENSMUST00000113567.10,NM_178884.5). The 1202th amino acids will be mutated from A to V, and the corresponding codon will be mutated to GTA by the GCA.

- The mouse *Obsl1*-202 transcript contains 20 exons. The translation initiation site ATG is located at exon1, and the translation termination site TAG is located at exon20, encoding 1804aa.

- The human NM_015311.3 transcript contains 21 exons. The translation initiation site ATG is located at exon1, and the translation termination site TAG is located at exon21, encoding 1896aa.

- In this project, *Obsl1* gene will be modified by CRISPR/Cas9 technology. The brief process is as follows: CRISPR/Cas9 system and donor were injected into the fertilized eggs of C57BL/6JGpt mice for homologous recombination, and obtained positive F0 mice identified by PCR and sequencing analysis. The stable inheritable positive F1 mice model was obtained by mating F0 mice with C57BL/6JGpt mice.

Notice

- According to the data of MGI, mice homozygous for a knock-out allele are embryonic lethal.

- The effect on transcript-201 is unknown.

- One or Two synonymous mutations of amino acids will be intronduced on exon11 of *Obsl1*.

- Mouse *Obsl1* gene is located on Chr2. Please take the loci in consideration when breeding this mutation mice with other gene modified strains, if the other gene is also on Chr2, it may be extremely hard to get double gene positive homozygotes.

- The scheme is designed according to the genetic information in the existing database. Due to the complex process of gene transcription and translation, it cannot be predicted completely at the present technology level.

The information of chr2:220422730:G:A(hg19,OBSL1)
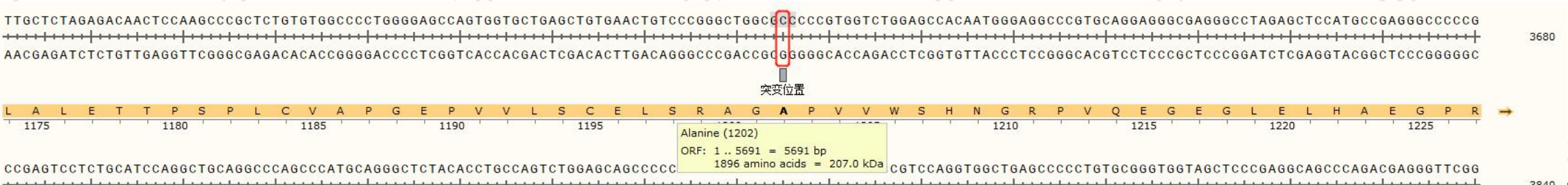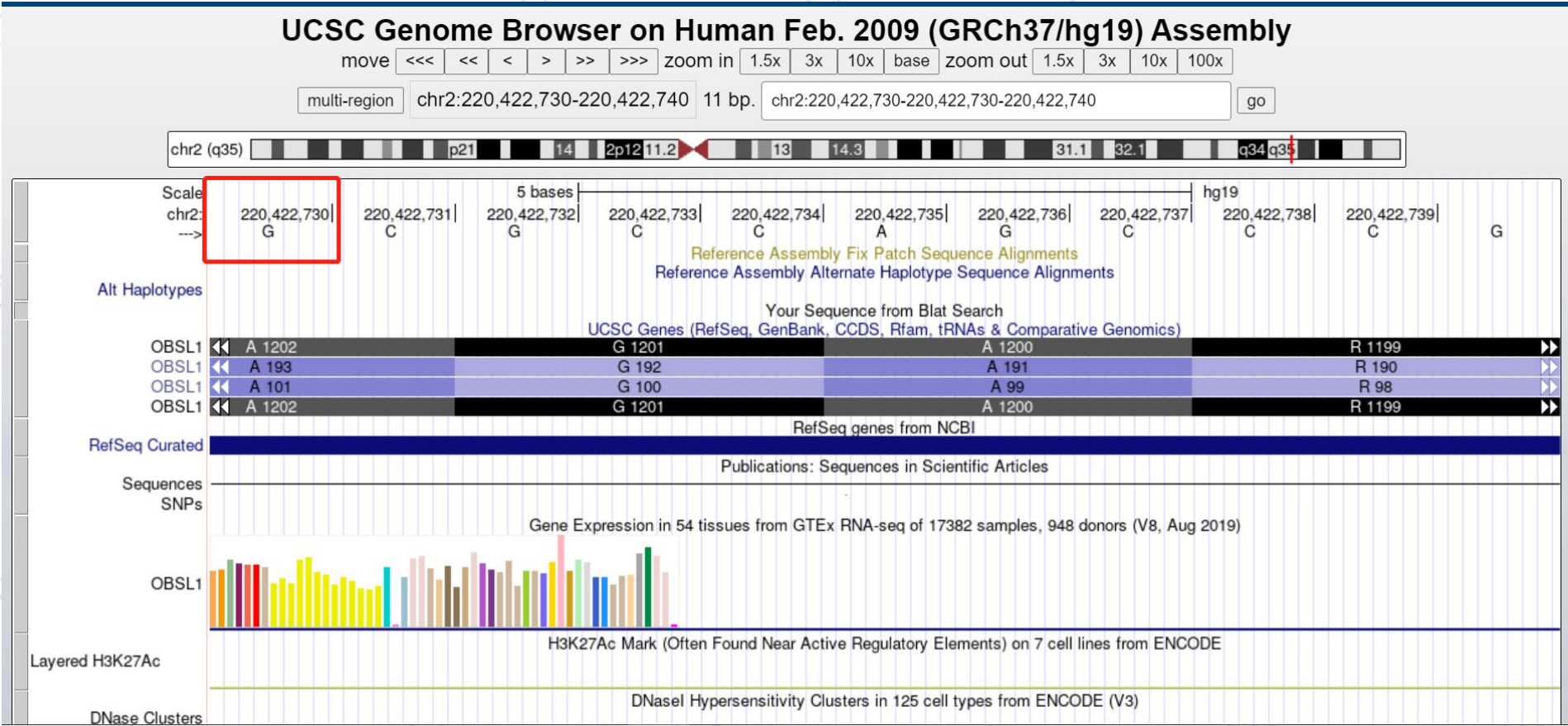
A comparison of the aa homology of human and mouse *Obsl1* gene

	1202	1200	1210	1220	1230	1240	1250	1260
Human aa	1202	APVVWSHNGRPVQEGEGLELHAEGPRRVLCIQAAGPAHAGLYTCQSGAAPGAPSLSFTVQVAEPPVRV
Mouse aa	1202	AQVFWSHNGSPVQQGEGLELRAEGPRRILCIQAADLAHTGVYTCQSGASPGAPSLSFNVQVAELPP--

consensus positions: 86.7%   identity positions: 83.9%

The 1202th amino acid(A) of human *OBSL1* gene(NM_015311.3) corresponds to the 1202th amino acid(A) of mouse *Obsl1* gene after comparing homology of mouse *Obsl1* gene and human *OBSL1* gene.

Targeted Mutation Site

Before mutation

After mutation

The blue region is coding sequence of exon11 of *Obsl1-202,* the yellow region represents the targeted mutation site.

Obsl1 obscurin-like 1 [*Mus musculus* (house mouse)]

Gene ID: 98733, updated on 23-Jun-2021

⬆ **Download Datasets**

Summary

Official Symbol	Obsl1 provided by MGI
Official Full Name	obscurin-like 1 provided by MGI
Primary source	MGI:MGI:2138628
See related	Ensembl:ENSMUSG00000026211
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	AW822216
Expression	Biased expression in ovary adult (RPKM 125.4), limb E14.5 (RPKM 44.0) and 9 other tissues See more
Orthologs	human all

NEW Try the new Gene table
Try the new Transcript table

Genomic context

Location: 1; 1 C4

See Obsl1 in Genome Data Viewer

Exon count: 22

Annotation release	Status	Assembly	Chr	Location
109	current	GRCm39 (GCF_000001635.27)	1	NC_000067.7 (75462469..75483143, complement)
108.20200622	previous assembly	GRCm38.p6 (GCF_000001635.26)	1	NC_000067.6 (75485825..75506486, complement)
Build 37.2	previous assembly	MGSCv37 (GCF_000001635.18)	1	NC_000067.5 (75482400..75503027, complement)

Chromosome 1 - NC_000067.7

[75426467 ▶   [75513979 ▶

Asic4   Obsl1   Stk11ip
Gm32506   Chpf   Inha
Tmem198
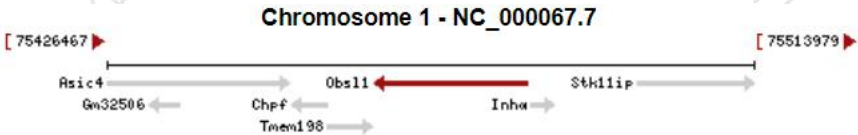
Transcript information(Ensembl)-*Obsl1*

The gene has 13 transcripts, and all the transcripts are shown below:

| Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt Match	Flags
Obsl1-202	ENSMUST00000113567.10	5679	1804aa	Protein coding	CCDS15077	D3YYU8-1	GENCODE basic APPRIS P1 TSL:1
Obsl1-201	ENSMUST00000113565.3	3379	1025aa	Protein coding	CCDS78624	A0A0B4J1L4	GENCODE basic TSL:1
Obsl1-211	ENSMUST00000155084.8	4131	1162aa	Protein coding	-	A0A0A0MQG1	TSL:2 CDS 5' incomplete
Obsl1-205	ENSMUST00000132252.2	1252	417aa	Protein coding	-	F7AGE9	TSL:5 CDS 5' and 3' incomplete
Obsl1-209	ENSMUST00000150293.2	341	No protein	Processed transcript	-	-	TSL:5
Obsl1-204	ENSMUST00000129403.8	2709	No protein	Retained intron	-	-	TSL:1
Obsl1-207	ENSMUST00000145306.2	2649	No protein	Retained intron	-	-	TSL:1
Obsl1-203	ENSMUST00000127507.8	2404	No protein	Retained intron	-	-	TSL:1
Obsl1-208	ENSMUST00000145382.2	724	No protein	Retained intron	-	-	TSL:2
Obsl1-212	ENSMUST00000156499.3	656	No protein	Retained intron	-	-	TSL:3
Obsl1-210	ENSMUST00000154636.2	651	No protein	Retained intron	-	-	TSL:3
Obsl1-206	ENSMUST00000138352.2	571	No protein	Retained intron	-	-	TSL:2
Obsl1-213	ENSMUST00000156705.2	440	No protein	Retained intron	-	-	TSL:3

The strategy is based on the design of *Obsl1*-202 transcript, the transcription is shown below:

< Obsl1-202
protein coding

Reverse strand

20.54 kb
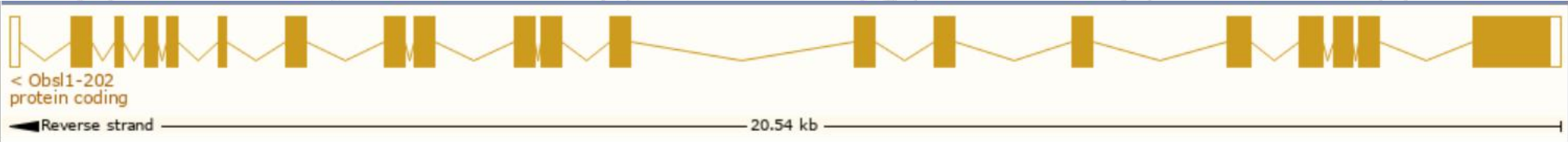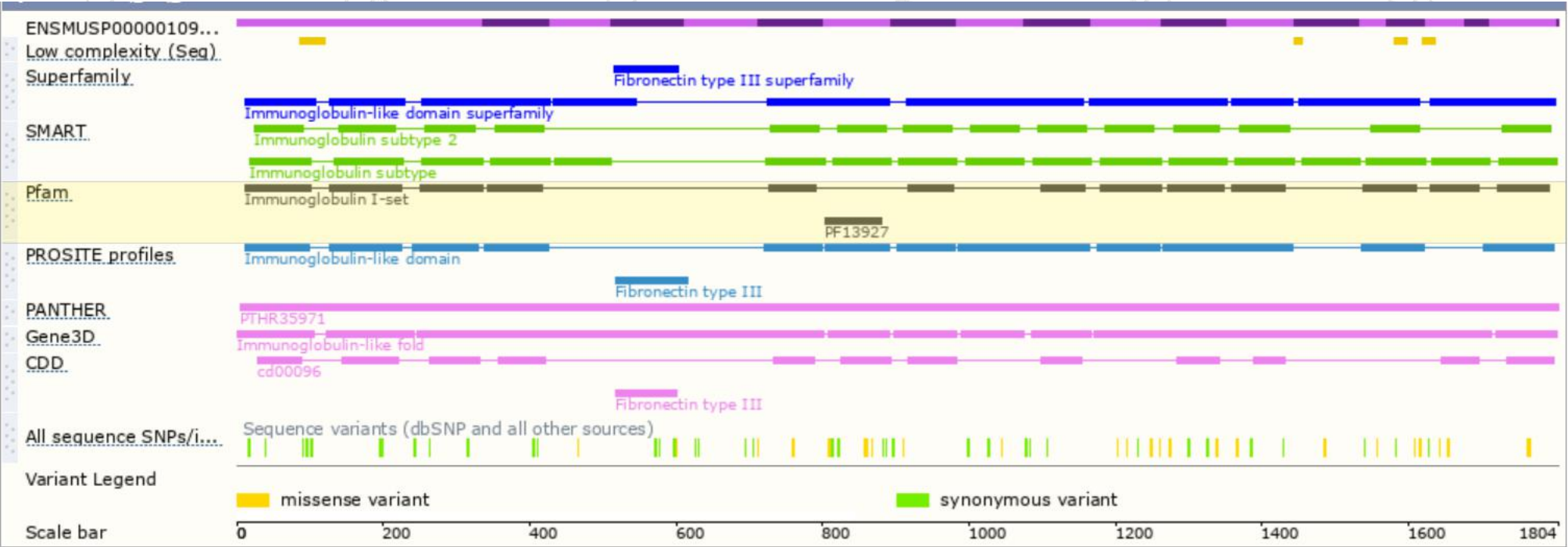
Genomic location distribution-*Obsl1*
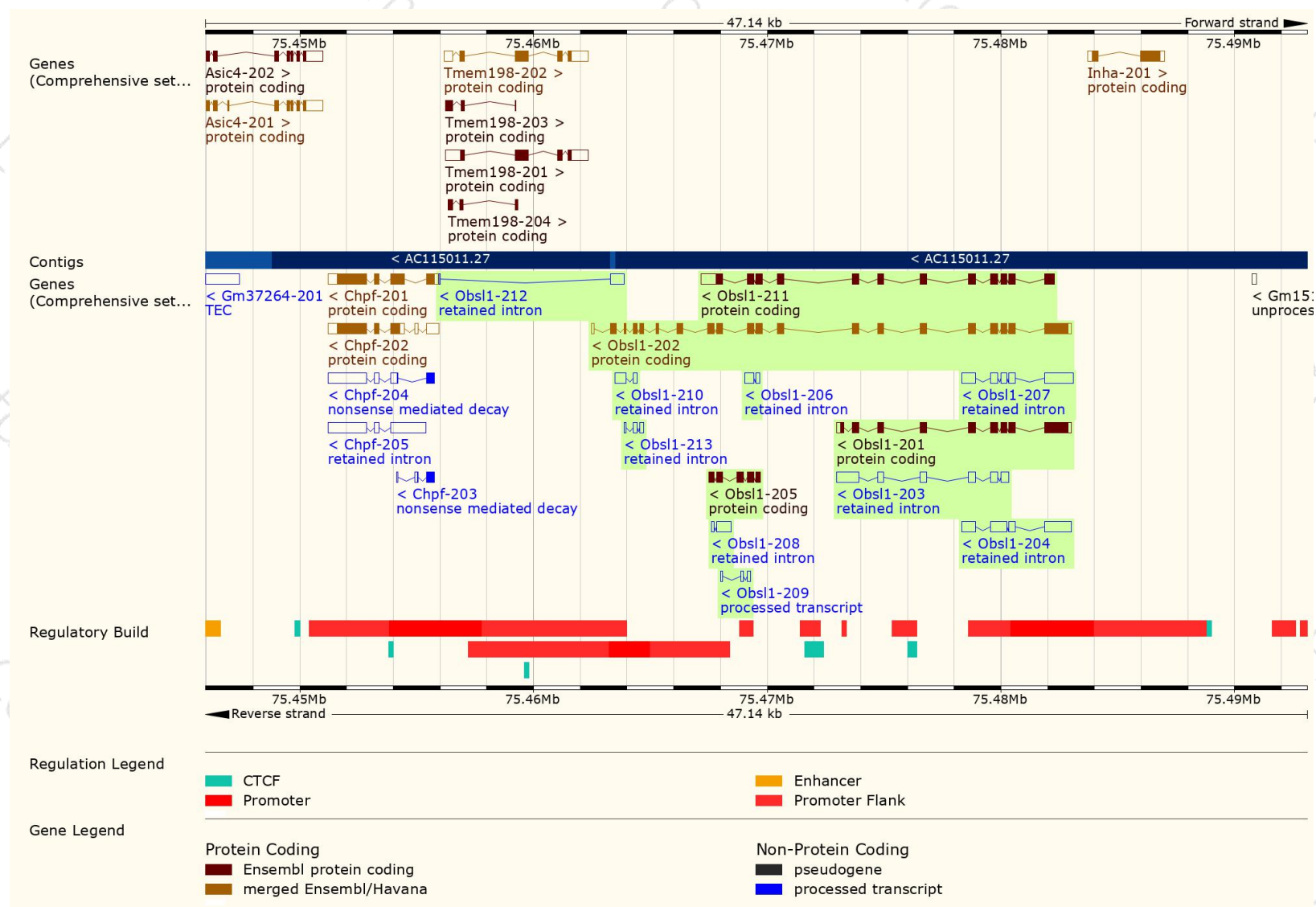
Protein domain-*Obsl1*

Mouse phenotype description(MGI)

URL link is as follows:
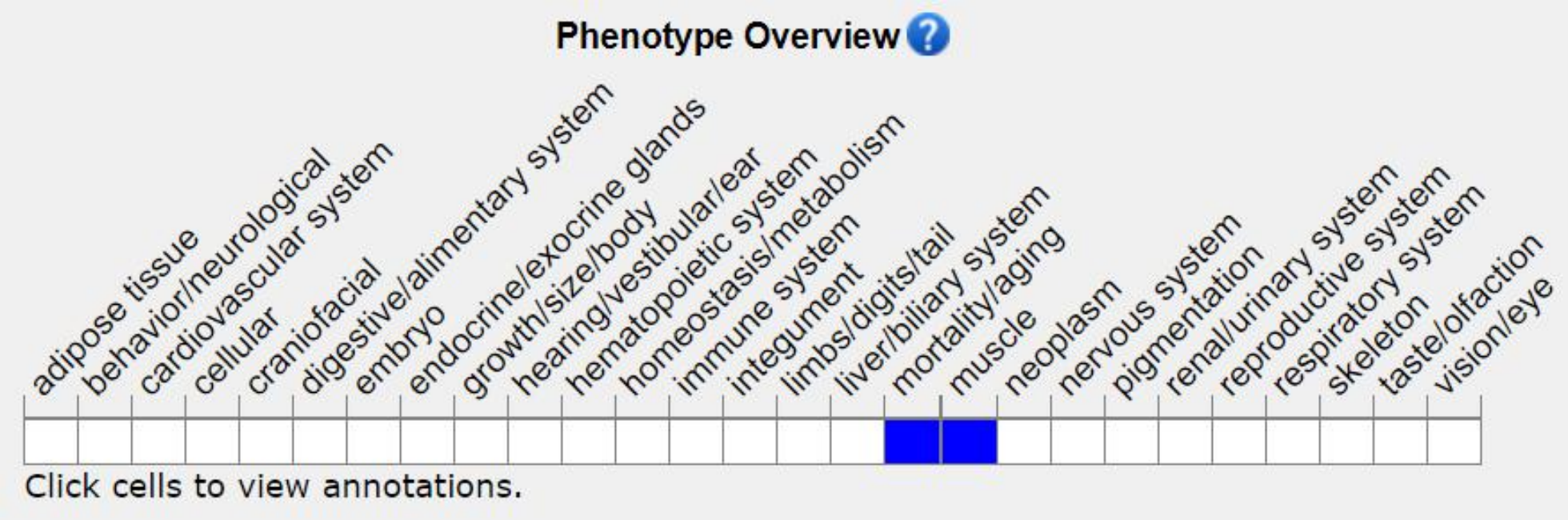
http://www.informatics.jax.org/marker/MGI:2138628

Mice homozygous for a knock-out allele are embryonic lethal.

OBSL1   obscurin like cytoskeletal adaptor 1 [*Homo sapiens* (human)]

⬇ Download Datasets

Gene ID: 23363, updated on 11-Jul-2021

▲ **Summary**   ⌃ ?

Official Symbol	OBSL1 provided by HGNC
Official Full Name	obscurin like cytoskeletal adaptor 1 provided by HGNC
Primary source	HGNC:HGNC:29092
See related	Ensembl:ENSG00000124006 MIM:610991
Gene type	protein coding
RefSeq status	REVIEWED
Organism	Homo sapiens
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
Summary	Cytoskeletal adaptor proteins function in linking the internal cytoskeleton of cells to the cell membrane. This gene encodes a cytoskeletal adaptor protein, which is a member of the Unc-89/obscurin family. The protein contains multiple N- and C-terminal immunoglobulin (Ig)-like domains and a central fibronectin type 3 domain. Mutations in this gene cause 3M syndrome type 2. Alternatively spliced transcript variants encoding different isoforms have been found in this gene. [provided by RefSeq, Mar 2010]
Expression	Broad expression in ovary (RPKM 37.4), testis (RPKM 15.3) and 19 other tissues See more
Orthologs	mouse all

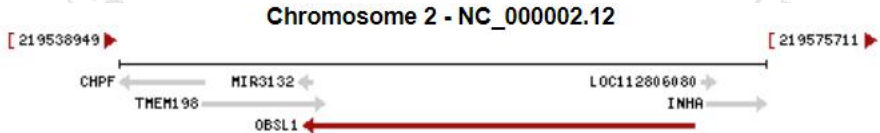**NEW** Try the new Gene table
Try the new Transcript table

▲ **Genomic context**   ⌃ ?

Location: 2q35

Exon count: 23

See OBSL1 in Genome Data Viewer

Annotation release	Status	Assembly	Chr	Location
109.20210514	current	GRCh38.p13 (GCF_000001405.39)	2	NC_000002.12 (219549408..219571573, complement)
105.20201022	previous assembly	GRCh37.p13 (GCF_000001405.25)	2	NC_000002.11 (220415450..220436261, complement)

Chromosome 2 - NC_000002.12

[219538949 ▶   [219575711 ▶

CHPF   MIR3132 ←   LOC112806080 →
   TMEM198   INHA →
              OBSL1 ←━━━━━━━━━━━━━━━━

The gene has 13 transcripts, and all the transcripts are shown below,the strategy is based on the design of NM_015311.3 transcript

If you have any questions, please feel free to contact us.
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