

Tpmt Cas9-KO Strategy

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Reviewer:

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Project Overview

Project Name

Tpmt

Project type

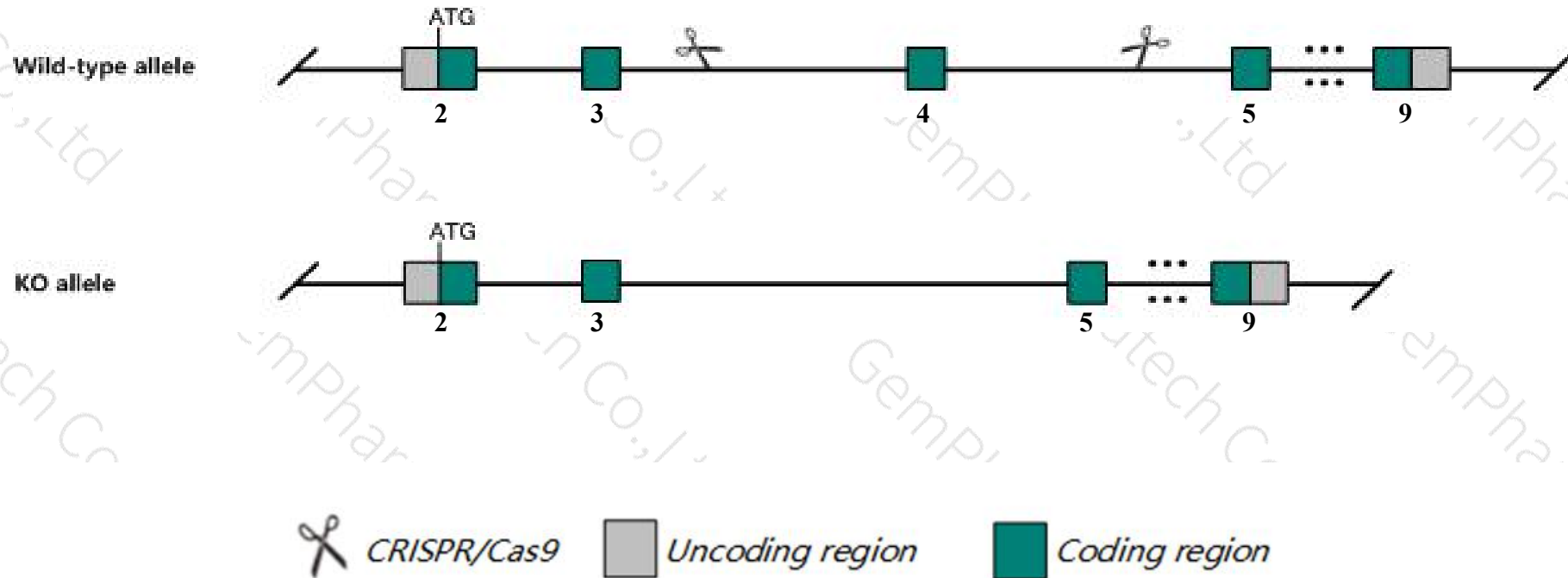
Cas9-KO

Strain background

C57BL/6JGpt

Knockout strategy

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



- The *Tpmt* gene has 8 transcripts. According to the structure of *Tpmt* gene, exon4 of *Tpmt-201* (ENSMUST00000021806.10) transcript is recommended as the knockout region. The region contains 133bp coding sequence. Knock out the region will result in disruption of protein function.
- In this project we use CRISPR/Cas9 technology to modify *Tpmt* gene. The brief process is as follows: CRISPR/Cas9 system were

- According to the existing MGI data, homozygous and heterozygous mutation of this gene results in increased sensitivity to mercaptopurine.
- The transcripts *Tpmt-203* and *Tpmt-208* are incomplete, so the effect on them are unknown.
- The *Tpmt* gene is located on the Chr13. 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)

Tpmt thiopurine methyltransferase [*Mus musculus* (house mouse)]

Gene ID: 22017, updated on 12-Aug-2019

Summary

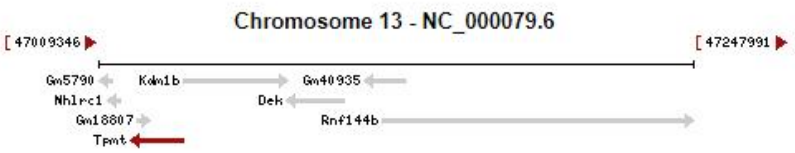
Official Symbol Tpmt provided by [MGI](#)
Official Full Name thiopurine methyltransferase provided by [MGI](#)
Primary source [MGI:MGI:98812](#)
See related [Ensembl:ENSMUSG00000021376](#)
Gene type protein coding
RefSeq status VALIDATED
Organism [Mus musculus](#)
Lineage Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as AW106912
Expression Broad expression in kidney adult (RPKM 7.3), genital fat pad adult (RPKM 5.0) and 23 other tissues [See more](#)
Orthologs [human](#) [all](#)

Genomic context

Location: 13 A5; 13 24.5 cM [See Tpmt in Genome Data Viewer](#)

Exon count: 11

Annotation release	Status	Assembly	Chr	Location
108	current	GRCm38.p6 (GCF_000001635.26)	13	NC_000079.6 (47021987..47043338, complement)
Build 37.2	previous assembly	MGSCv37 (GCF_000001635.18)	13	NC_000079.5 (47118912..47138586, complement)

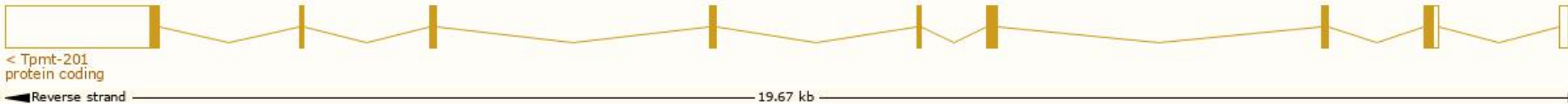


Transcript information (Ensembl)

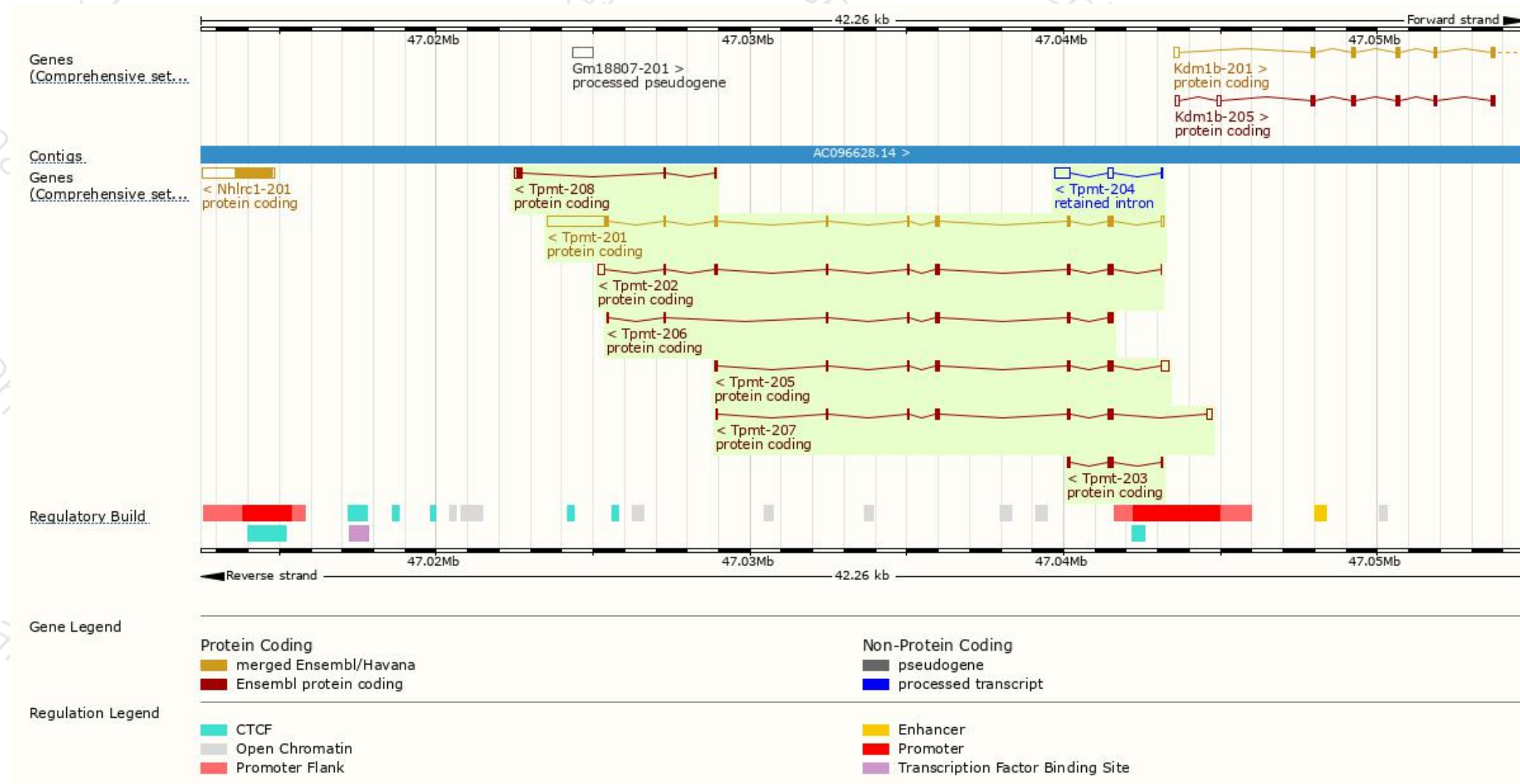
The gene has 8 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Tpmt-201	ENSMUST00000021806.10	2708	240aa	Protein coding	CCDS26488	A0A0R4J018	TSL:1 GENCODE basic APPRIS P1
Tpmt-202	ENSMUST00000110118.7	881	205aa	Protein coding	-	D3Z380	TSL:1 GENCODE basic
Tpmt-205	ENSMUST00000136864.7	838	188aa	Protein coding	-	D3YWK6	CDS 3' incomplete TSL:5
Tpmt-207	ENSMUST00000154802.1	779	182aa	Protein coding	-	D3Z217	CDS 3' incomplete TSL:3
Tpmt-206	ENSMUST00000151509.8	609	188aa	Protein coding	-	D6RIK3	CDS 5' incomplete TSL:5
Tpmt-208	ENSMUST00000224970.1	338	83aa	Protein coding	-	A0A286YCA5	CDS 5' incomplete
Tpmt-203	ENSMUST00000124948.1	315	93aa	Protein coding	-	D3Z0R1	CDS 3' incomplete TSL:3
Tpmt-204	ENSMUST00000133100.1	698	No protein	Retained intron	-	-	TSL:1

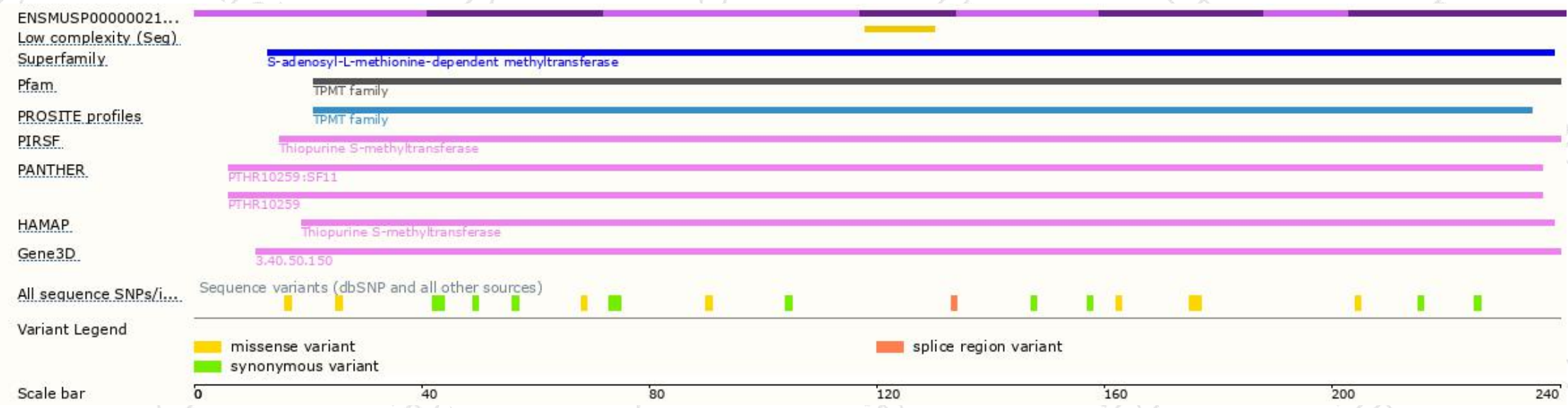
The strategy is based on the design of *Tpmt-201* transcript, the transcription is shown below:



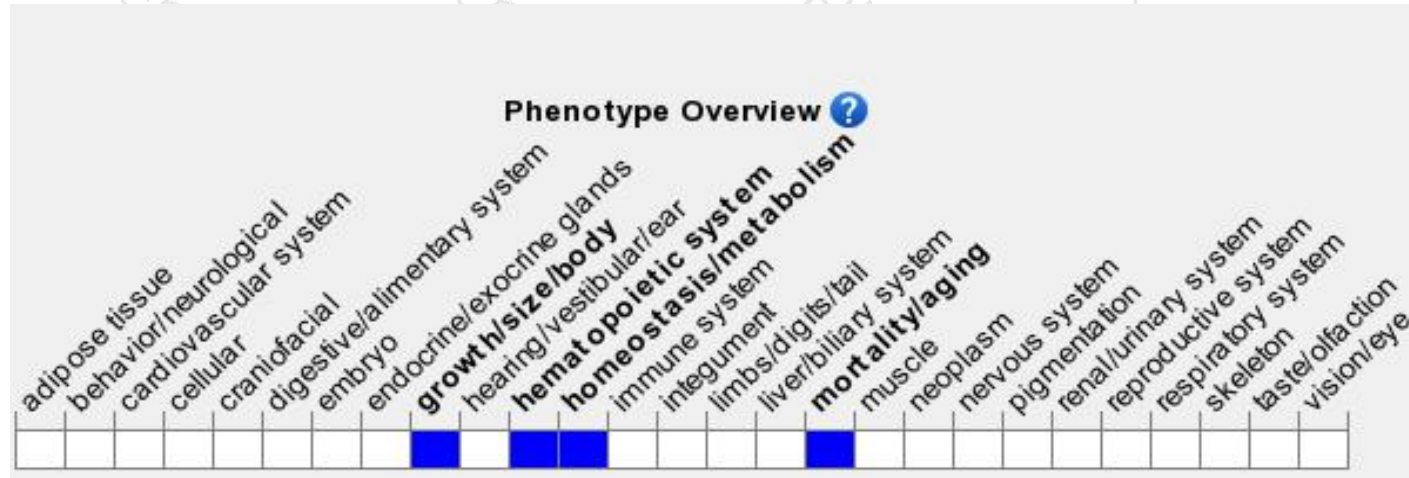
Genomic location distribution



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 and heterozygous mutation of this gene results in increased sensitivity to mercaptopurine.

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

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