Tcf7l2 Cas9-CKO Strategy

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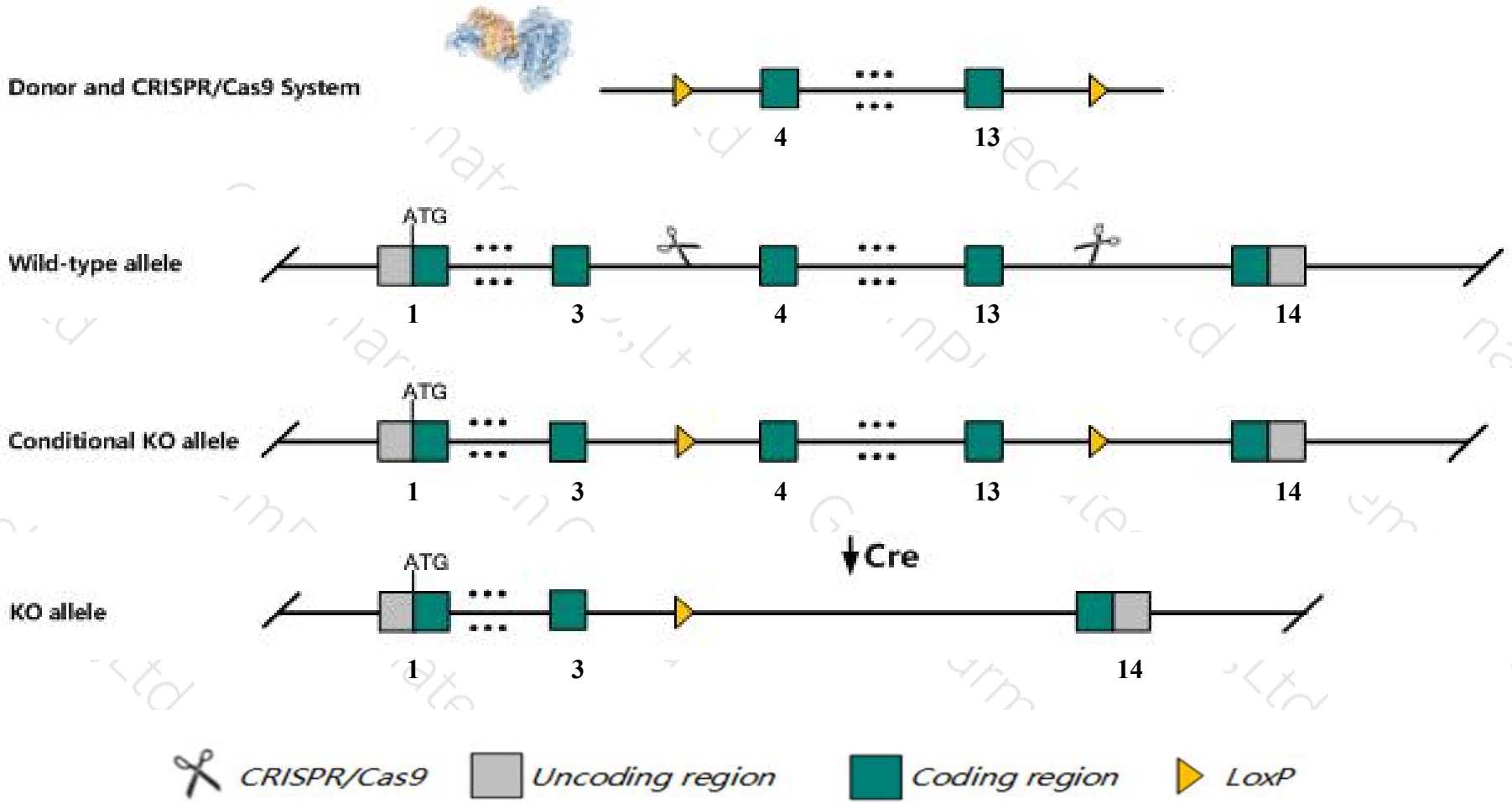
Project Overview

Project Name	***Tcf7l2***
Project type	**Cas9-CKO**
Strain background	**C57BL/6JGpt**

Conditional Knockout strategy

This model will use CRISPR/Cas9 technology to edit the *Tcf7l2* gene. The schematic diagram is as follows:



Technical routes

- The *Tcf7l2* gene has 22 transcripts. According to the structure of *Tcf7l2* gene, exon4-exon13 of *Tcf7l2-209* (ENSMUST00000111656.7) transcript is recommended as the knockout region.The region contains 992bp coding sequence. Knock out the region will result in disruption of protein function.

- In this project we use CRISPR/Cas9 technology to modify *Tcf7l2* 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 sequencing. A stable F1 generation mouse model was obtained by mating positive F0 generation mice with C57BL/6JGpt mice.

- 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.

Notice

- According to the existing MGI data,Animals homozygous for a targeted mutation exhibit intestinal epithelia abnormalities and die shortly after birth. Mice heterozygous for some mutations display abnormalities in glucose homeostasis.

- The *Tcf7l2* gene is located on the Chr19. 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 loxp insertion on gene transcription, RNA splicing and protein translation cannot be predicted at existing technological level.

Gene information （NCBI）

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Tcf7l2 transcription factor 7 like 2, T cell specific, HMG box [Mus musculus (house mouse)]

Gene ID: 21416, updated on 5-Mar-2019

Summary

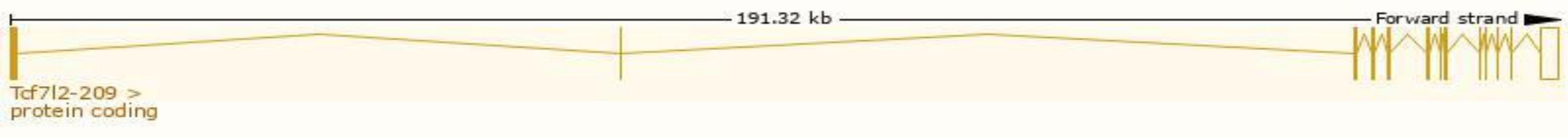
Official Symbol	Tcf7l2 provided by MGI
Official Full Name	transcription factor 7 like 2, T cell specific, HMG box provided by MGI
Primary source	MGI:MGI:1202879
See related	Ensembl:ENSMUSG00000024985
Gene type	protein coding
RefSeq status	VALIDATED
Organism	Mus musculus
Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as	TCF4B, TCF4E, Tcf-4, Tcf4
Expression	Broad expression in whole brain E14.5 (RPKM 35.3), CNS E14 (RPKM 21.4) and 25 other tissues See more
Orthologs	human all

Transcript information（Ensembl）

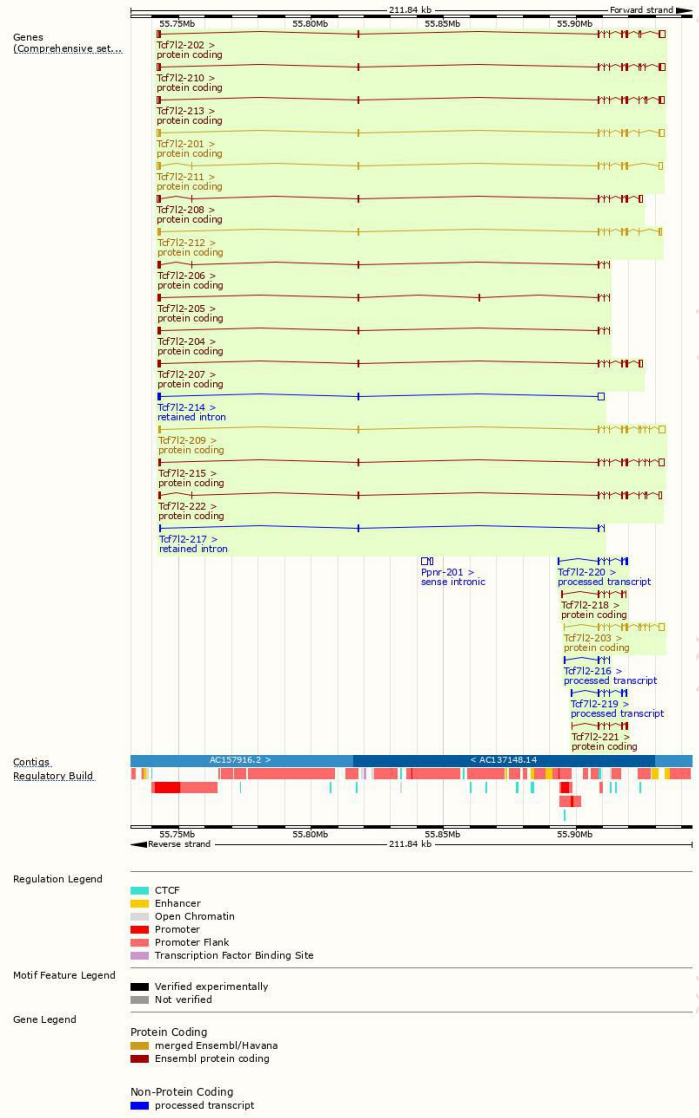
The gene has 22 transcripts,all transcripts are shown below:

Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Tcf7l2-209	ENSMUST00000111656.7	3629	459aa	Protein coding	CCDS50471	E9QQ91	TSL:1 GENCODE basic APPRIS ALT2
Tcf7l2-201	ENSMUST00000041717.13	3590	442aa	Protein coding	CCDS50473	D3YWT3	TSL:1 GENCODE basic APPRIS ALT2
Tcf7l2-202	ENSMUST00000061496.16	3193	459aa	Protein coding	CCDS29911	F6WBK9	TSL:5 GENCODE basic APPRIS P3
Tcf7l2-211	ENSMUST00000111658.9	3012	435aa	Protein coding	CCDS50469	E9Q990	TSL:1 GENCODE basic
Tcf7l2-203	ENSMUST00000111646.7	2839	299aa	Protein coding	CCDS50474	Q924A0	TSL:1 GENCODE basic
Tcf7l2-212	ENSMUST00000111659.8	2324	447aa	Protein coding	CCDS50470	A0A0R4J1G0	TSL:1 GENCODE basic
Tcf7l2-210	ENSMUST00000111657.10	2135	598aa	Protein coding	CCDS50472	E9QQ90	TSL:5 GENCODE basic
Tcf7l2-213	ENSMUST00000111662.10	3715	606aa	Protein coding	-	E9QQ89	TSL:5 GENCODE basic
Tcf7l2-215	ENSMUST00000127233.8	3220	442aa	Protein coding	-	F6WPX2	TSL:1 GENCODE basic
Tcf7l2-222	ENSMUST00000153888.8	2318	477aa	Protein coding	-	F6XQR1	TSL:5 GENCODE basic
Tcf7l2-221	ENSMUST00000148666.1	800	265aa	Protein coding	-	D3Z1L0	CDS 3' incomplete TSL:3
Tcf7l2-218	ENSMUST00000142291.7	729	178aa	Protein coding	-	D3Z002	CDS 3' incomplete TSL:3
Tcf7l2-220	ENSMUST00000145249.7	830	No protein	Processed transcript	-	-	TSL:3
Tcf7l2-219	ENSMUST00000143334.1	746	No protein	Processed transcript	-	-	TSL:3
Tcf7l2-216	ENSMUST00000127653.7	395	No protein	Processed transcript	-	-	TSL:3
Tcf7l2-208	ENSMUST00000111654.7	3059	No protein	Retained intron	-	-	TSL:2
Tcf7l2-214	ENSMUST00000126434.7	2683	No protein	Retained intron	-	-	TSL:2
Tcf7l2-207	ENSMUST00000111653.7	2629	No protein	Retained intron	-	-	TSL:2
Tcf7l2-205	ENSMUST00000111651.7	1127	No protein	Retained intron	-	-	TSL:1
Tcf7l2-206	ENSMUST00000111652.8	1087	No protein	Retained intron	-	-	TSL:1
Tcf7l2-204	ENSMUST00000111649.7	982	No protein	Retained intron	-	-	TSL:1
Tcf7l2-217	ENSMUST00000133008.7	691	No protein	Retained intron	-	-	TSL:5

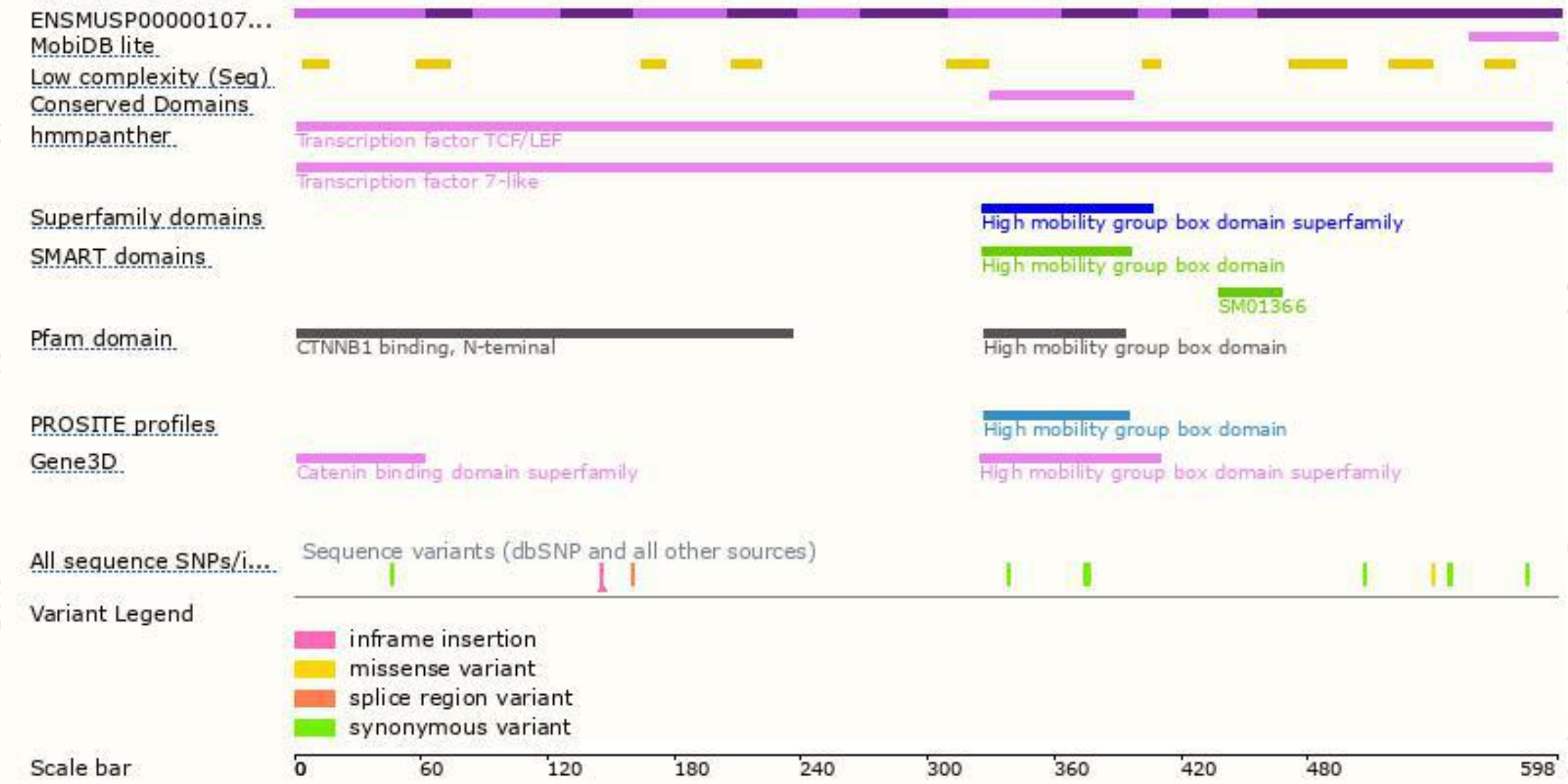
The strategy is based on the design of *Tcf7l2-209* transcript,The transcription is shown below



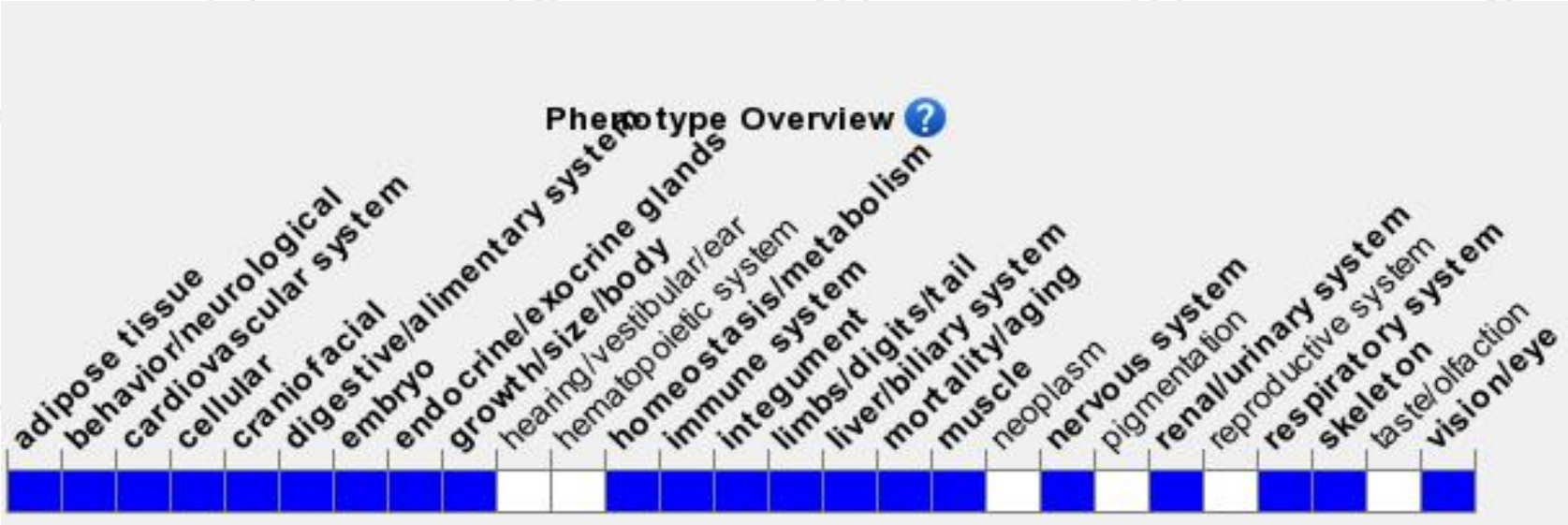
Genomic location distribution



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,Animals homozygous for a targeted mutation exhibit intestinal epithelia abnormalities and die shortly after birth. Mice heterozygous for some mutations display abnormalities in glucose homeostasis

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

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