

Htt Cas9-KO Strategy

Designer: Xiaojing Li

Design Date: 2019-9-16

Reviewer: JiaYu

Project Overview



Project Name Htt

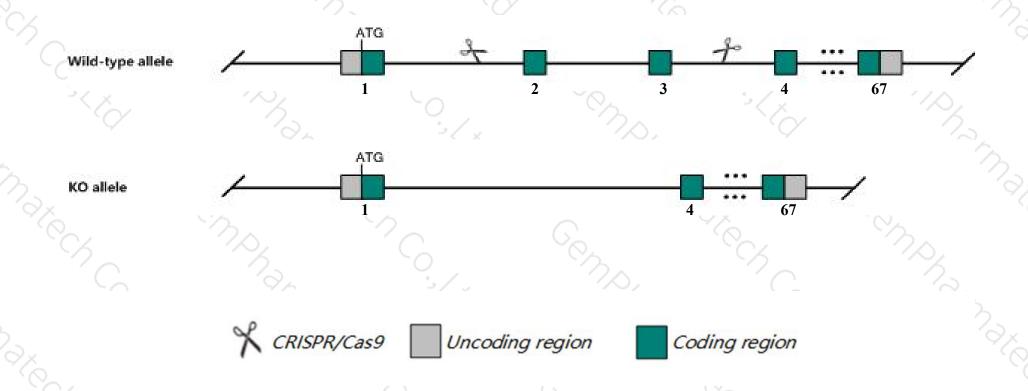
Project type Cas9-KO

Strain background C57BL/6JGpt

Knockout strategy



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



Technical routes



- ➤ The *Htt* gene has 8 transcripts. According to the structure of *Htt* gene, exon2-exon3 of *Htt-201*(ENSMUST00000080036.2) transcript is recommended as the knockout region. The region contains 205bp coding sequence.

 Knock out the region will result in disruption of protein function.
- ➤ In this project we use CRISPR/Cas9 technology to modify *Htt* gene. The brief process is as follows: CRISPR/Cas9 system we

Notice



- ➤ According to the existing MGI data, Null mutants gastrulate abnormally and die in utero. Conditional mutants are small with progressive neurodegeneration. Knock-ins of 20-150 CAG repeat units variably mimic Huntingtons with late-onset motor defects, reactive gliosis and neuronal inclusions.
- > The *Htt* gene is located on the Chr5. 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)



Htt huntingtin [Mus musculus (house mouse)]

Gene ID: 15194, updated on 30-Mar-2019

Summary

☆ ?

Official Symbol Htt provided by MGI

Official Full Name huntingtin provided by MGI

Primary source MGI:MGI:96067

See related Ensembl: ENSMUSG00000029104

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 Al256365, C430023I11Rik, Hd, Hdh, IT15

Expression Ubiquitous expression in cerebellum adult (RPKM 10.2), cortex adult (RPKM 9.1) and 28 other tissuesSee more

Orthologs human all

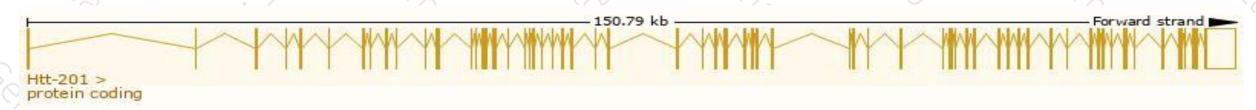
Transcript information (Ensembl)



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

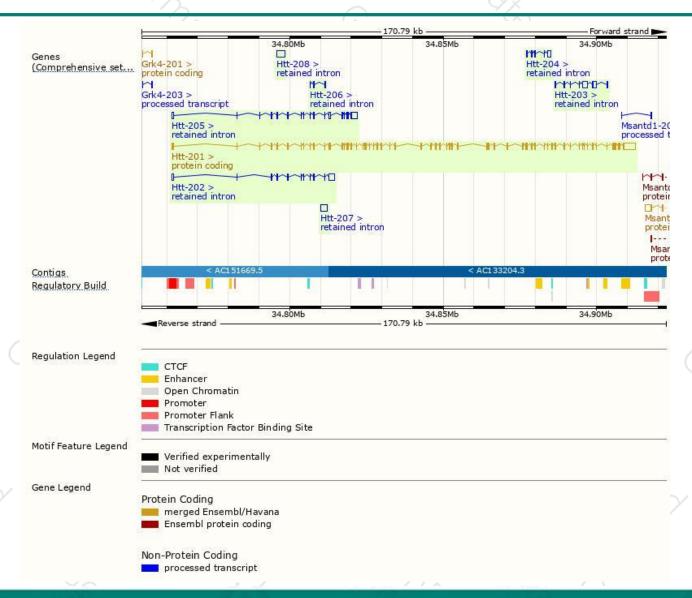
Name	Transcript ID	bp	Protein	Biotype	CCDS	UniProt	Flags
Htt-201	ENSMUST00000080036.2	13215	3120aa	Protein coding	CCDS19220	G3X9H5	TSL:1 GENCODE basic APPRIS P1
Htt-205	ENSMUST00000148953.7	4382	No protein	Retained intron	141	197	TSL:1
Htt-203	ENSMUST00000124272.1	3976	No protein	Retained intron	828	84	TSL:1
Htt-202	ENSMUST00000123755.7	3225	No protein	Retained intron	1928	4	TSL:1
Htt-208	ENSMUST00000202059.1	2614	No protein	Retained intron	(8)	85	TSL:NA
Htt-207	ENSMUST00000201613.1	2271	No protein	Retained intron	-	15 .	TSL:NA
Htt-204	ENSMUST00000135039.1	1570	No protein	Retained intron	828	84	TSL:1
Htt-206	ENSMUST00000156490.1	457	No protein	Retained intron	525	82	TSL:3

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



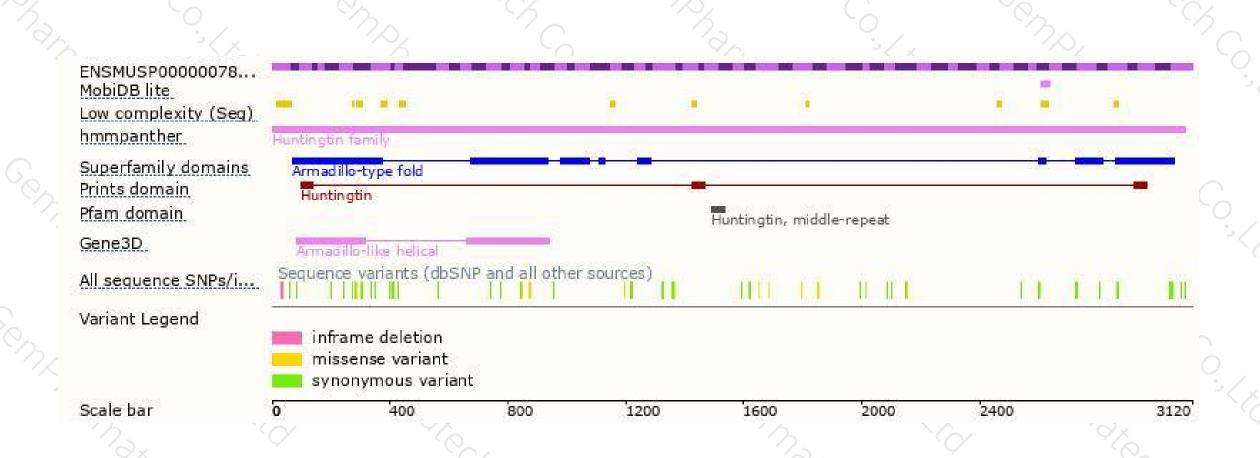
Genomic location distribution





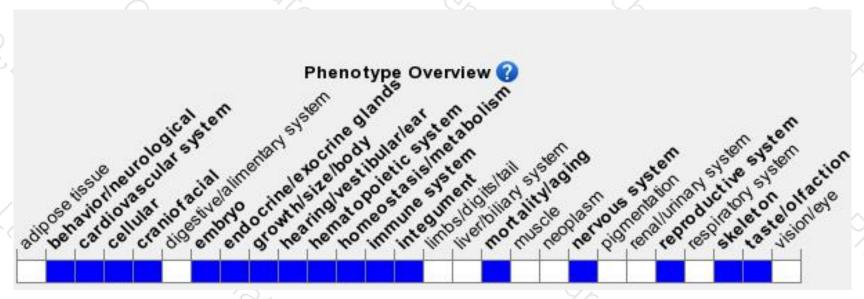
Protein domain





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, Null mutants gastrulate abnormally and die in utero. Conditional mutants are small with progressive neurodegeneration. Knock-ins of 20-150 CAG repeat units variably mimic Huntingtons with late-onset motor defects, reactive gliosis and neuronal inclusions.



If you have any questions, you are welcome to inquire. Tel: 400-9660890





