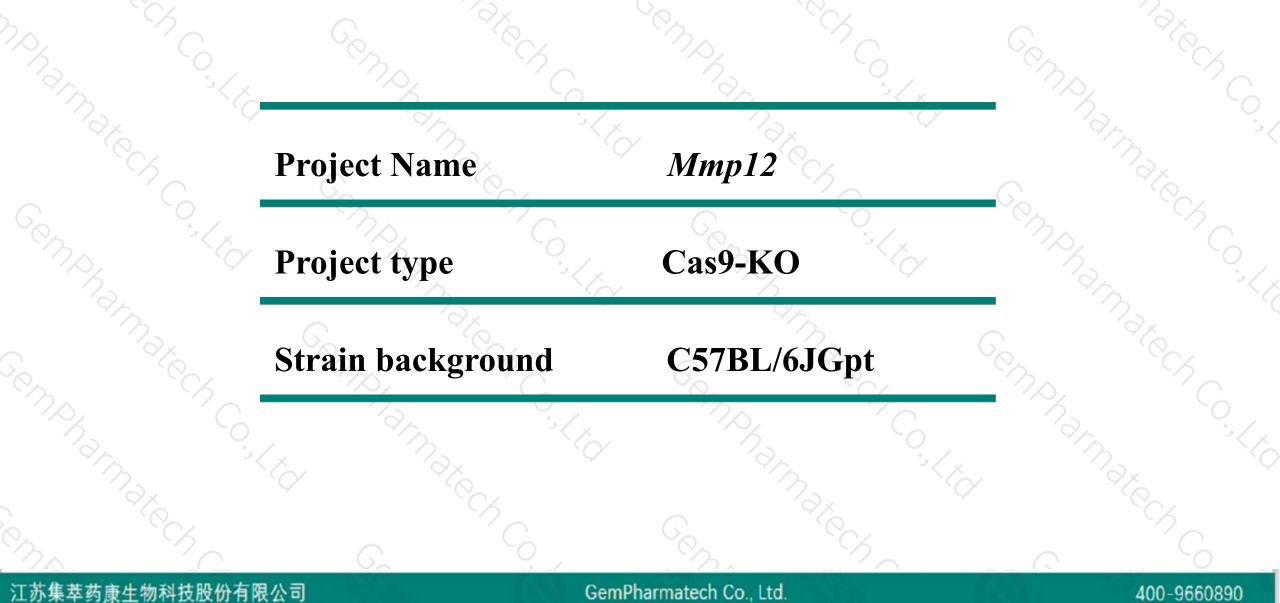


Mmp12 Cas9-KO Strategy

Designer: Reviewer: Design Date: Huimin Su Ruirui Zhang 2020/1/16

Project Overview

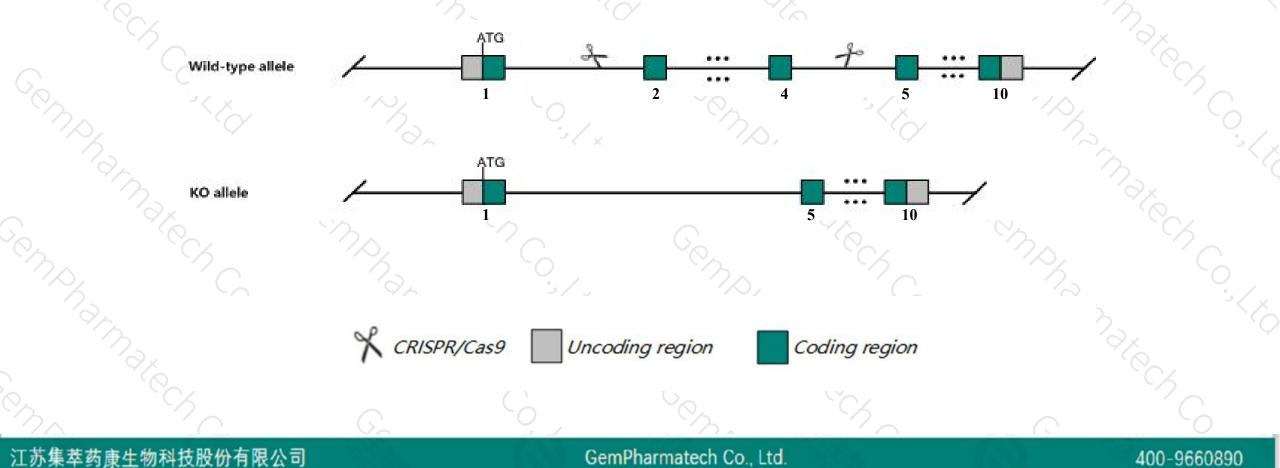




Knockout strategy



This model will use CRISPR/Cas9 technology to edit the Mmp12 gene. The schematic diagram is as follows:





- The Mmp12 gene has 7 transcripts. According to the structure of Mmp12 gene, exon2-exon4 of Mmp12-201 (ENSMUST0000005950.11) transcript is recommended as the knockout region. The region contains 523bp coding sequence. Knock out the region will result in disruption of protein function.
- > In this project we use CRISPR/Cas9 technology to modify Mmp12 gene. The brief process is as follows: CRISPR/Cas9 system

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- According to the existing MGI data, Mice homozygous for a knock-out allele exhibit decreased sensitivity to cigarette smoke, decreased littler size, abnormal myelination, abnormal macrophage physiology, and decreased oligodedrocytes.
- The Mmp12 gene is located on the Chr9. 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.

Notice

Gene information (NCBI)



< ?

Mmp12 matrix metallopeptidase 12 [Mus musculus (house mouse)]

Gene ID: 17381, updated on 10-Oct-2019

Summary

Official Symbol	Mmp12 provided by MGI									
Official Full Name	matrix metallopeptidase 12 provided by MGI									
Primary source	MGI:MGI:97005									
See related	Ensembl:ENSMUSG0000049723									
Gene type	e 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	MME; Mmel; AV378681									
Summary	This gene encodes a member of the matrix metalloproteinase family of extracellular matrix-degrading enzymes that are involved in tissue remodeling, wound repair, progression of atherosclerosis and tumor invasion. The encoded preproprotein undergoes proteolytic processing to generate a mature, zinc-dependent endopeptidase enzyme. Mice lacking the encoded protein have a diminished capacity to degrade extracellular matrix components, do not develop emphysema in response to long-term exposure to cigarette smoke, and exhibit impaired clearance and increased mortality upon bacterial infection. This gene is located in a cluster of other matrix metalloproteinase genes on chromosome 9. Alternate splicing generates multiple transcript variants encoding distinct isoforms. [provided by RefSeq, Feb 2016]									
Expression	Low expression observed in reference dataset See more									
Orthologs	human all									
	$\sim \sim $									

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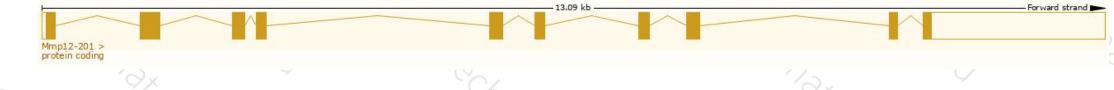
Transcript information (Ensembl)



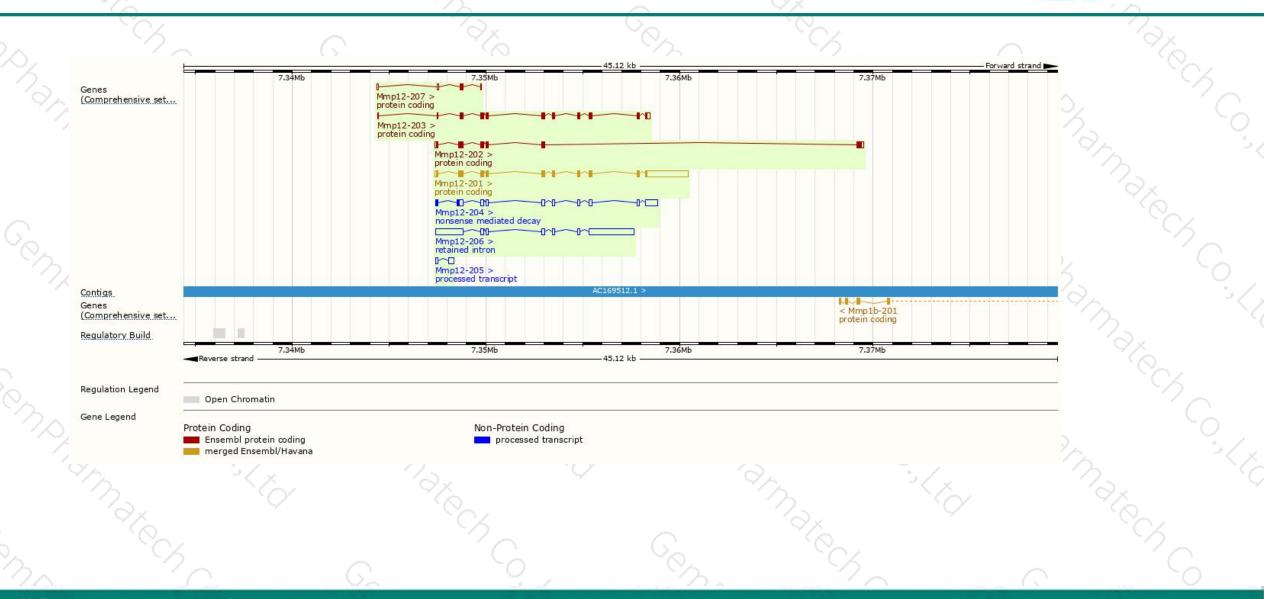
The gene has 7 transcripts, all transcripts are shown below:

Name 🎍	Transcript ID	bp 🍐	Protein 🛓	Biotype 💧	CCDS	UniProt 💧	Flags			
Mmp12-201	ENSMUST0000005950.11	3607	<u>473aa</u>	Protein coding	<u>CCDS22804</u> &	<u>P34960</u> @	TSL:1 GENCODE basic APPRIS P3			
Mmp12-203	ENSMUST00000120655.7	1452	<u>403aa</u>	Protein coding	<u>CCDS85639</u> മ	<u>Q3TCW6</u> &	TSL:1 GENCODE basic APPRIS ALT2			
Mmp12-202	ENSMUST0000065079.5	1185	<u>339aa</u>	Protein coding	- <u>Q8BJC0</u> ଜ		TSL:1 GENCODE basic			
Mmp12-207	ENSMUST00000150167.1	362	<u>72aa</u>	Protein coding - D3Z705&		CDS 3' incomplete TSL:5				
Mmp12-204	ENSMUST00000127722.1	2060	<u>64aa</u>	Nonsense mediated decay	nse mediated decay - <u>D6RJI9</u> 교		TSL:1			
Mmp12-205	ENSMUST00000138220.1	410	No protein	Processed transcript	12	0.53	TSL:2			
Mmp12-206	Mmp12-206 ENSMUST00000148005.7 4474 No pr		No protein	Retained intron	9 7		TSL:1			

The strategy is based on the design of *Mmp12-201* transcript, The transcription is shown below



Genomic location distribution



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Protein domain



	ENSMUSP00000005				60	ns.		° K	\cap		G.	0		8
5	Low complexity (Seg) Cleavage site (Sign Superfamily	PGBD-like superfamily	SSF55486				н	emopexin-like	e domain su					S.
	SMART Prints Pfam.	Peptidoglycan binding-like	Peptidase, metallop Peptidase M10A e Peptidase M10, m			-		1112112	in-like repei in-like repei					
	PROSITE profiles PROSITE patterns		Peptidase M10A, cysteine	switch, zinc binding	site			Hemopexin	-like repeat Hem	s opexin, conserv	ed site			
	PIRSE PANTHER Gene3D	Peptidase M10A Macrophage metalloelastase PTHR10201										3		
	CDD.	Metallopeptidase, catalytic d	Metallopeptidase, catalytic domain superfamily Peptidase M10A, catalytic domain						Hemopexin-like domain superfamily Hemopexin-like domain					
	All sequence SNPs/i	Sequence variants (dbSNP and all o	ther sources)		1 0	10				a ()			(0
	Variant Legend	missense variant	missense variant missense variant					synonymous variant						- 57
	Scale bar	o 40 i	30 120	160	200	240	28		320	36		400	473	
	~ 2	<u> </u>		0		%.		9	2~		(0	G)

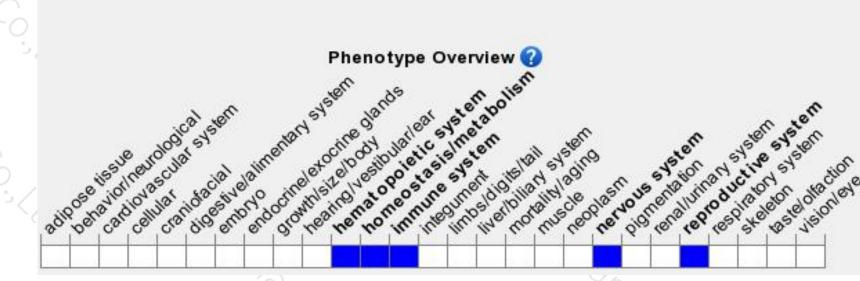
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Mouse phenotype description(MGI)





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, Mice homozygous for a knock-out allele exhibit decreased sensitivity to cigarette smoke, decreased littler size, abnormal myelination, abnormal macrophage physiology, and decreased oligodedrocytes.



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



