

**B6.Cg-Adamts4<sup>em1Adiuj</sup> Apoe<sup>tm1.1(APOE\*4)Adiuj</sup> App<sup>em1Adiuj</sup> Trem2<sup>em1Adiuj</sup> /J**

Stock No: **033868** | Adamts4 enhancer KO/hAbeta/APOE4/Trem2\*R47H

 Congenic, Endonuclease-Mediated Mutation, Targeted Mutation

Estimated to begin distribution on May 3, 2021

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locus. This deletes a conserved microglia enhancer region, including a variant (rs4575098) linked to risk of Alzheimer's disease.

This mutation is maintained with the hAbeta/APOE4/Trem2\*R47H mutations (Stock No. [030670](#)) intended to increase risk of late-onset Alzheimer's disease: a humanized *Apoe* knock-in mutation (sequence coding for human isoform E4), a CRISPR/*cas9*-generated *App* allele with a humanized Abeta1-42 region (G601R, F606Y, R609H in the mouse gene, corresponding to amino acid positions 676, 681, 684 in the human *APP* locus) and a CRISPR/*cas9*-generated R47H point mutation of the *Trem2* gene.

### Donating Investigator

Mike Sasner, The Jackson Laboratory

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## GENETIC OVERVIEW

### Genetic Background

### Generation

#### *Trem2<sup>em1Adiuj</sup>*

##### Allele Type

Endonuclease-mediated  
(Humanized sequence)

##### Gene Symbol

*Trem2*

##### Gene Name

triggering receptor expressed on myeloid cells 2

#### *Apoe<sup>tm1.1(APOE\*4)Adiuj</sup>*

##### Allele Type

Targeted (Inserted  
expressed sequence,  
Humanized sequence)

##### Gene Symbol

*Apoe*

##### Gene Name

apolipoprotein E

#### *App<sup>em1Adiuj</sup>*

##### Allele Type

Endonuclease-mediated

##### Gene Symbol

*App*

##### Gene Name

amyloid beta (A4) precursor protein

(Humanized sequence)

*Adamts4<sup>em1Aduj</sup>*

Alele Type	Gene Symbol	Gene Name
Endonuclease-mediated (Not Specified)	<i>Adamts4</i>	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 4

[VIEW GENETICS](#)

## RESEARCH APPLICATIONS

Neurobiology Research  
Mouse/Human Gene Homologs  
Research Tools  
Cardiovascular Research  
Metabolism Research

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## BASE PRICE

Starting at:

\$255.00 Domestic price for female

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### [Details](#)

#### [Detailed Description](#)

This *Adamts4* enhancer KO/hAbeta/APOE4/*Trem2*\*R47H quadruple mutant strain carries an *Adamts4* enhancer deletion allele where the 2 kb region of *Fcer1g* enhancer (including SNPs rs4575098 and rs11585858) is deleted, a humanized ApoE knock-in allele in which exons 2, 3 and most of exon 4 of the mouse *ApoE* gene were replaced by human *APOE4* gene sequence including exons 2, 3 and 4 (and some 3' UTR sequence), a mutant allele of the *App* gene containing G601R, F606Y and R609H point mutations, and a knock-in of a point mutation into mouse *Trem2* gene containing an R47H point mutation with two silent mutations.

The targeted *Adamts4* gene encodes a zinc-dependent protease involved in aggrecan degradation. The targeted *ApoE* gene encodes apolipoprotein E, which is important in lipoprotein metabolism and cardiovascular disease as well as Alzheimer's disease, immunoregulation and cognition. The targeted *App* gene encodes amyloid beta precursor protein, a transmembrane cell surface receptor that is cleaved by secretases. Mutations in this gene have been associated with Alzheimer's disease. The targeted *Trem2* gene (triggering receptor expressed on myeloid cells 2) encodes a protein that is part of a receptor signaling complex with TYRO protein tyrosine kinase binding protein, and that activates macrophages and dendritic cells during immune responses. The *TREM2* R47H mutation is a missense mutation in exon 2 that is one of the strongest genetic risk factors for late-onset Alzheimer's disease.

Mice that are homozygous for *Adamts4*<sup>em1Aduj</sup> (*Adamts4* enhancer KO), *ApoE*<sup>tm1.1(APOE\*4)Aduj</sup> (*APOE4*), *App*<sup>em1Aduj</sup> (*hAbeta*) and *Trem2*<sup>em1Aduj</sup> (*Trem2*\*R47H) are viable and fertile [March 2020]. If additional characterization of these *Adamts4* enhancer KO/*hAbeta*/*APOE4*/*Trem2*\*R47H mice is performed, we may modify the strain description accordingly.

Of note, in brains of mice homozygous for the *Trem2*<sup>em1Aduj</sup> allele (and not carrying any other mutant alleles), expression of both transcripts of *Trem2* is decreased by about 50%. Mice expressing the *Trem2* R47H mutation also express a novel splice variant with a deletion of 119bp at the 5' end of exon 2, due to a cryptic splice acceptor site in exon 2 (see Stock No. 027918).

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## + Development

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## + Expression Data

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## + Control Suggestions

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## - Genetics

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### + *Trem2*<sup>em1Aduj</sup>

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### + *ApoE*<sup>tm1.1(APOE\*4)Aduj</sup>

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### + *App*<sup>em1Aduj</sup>

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### + *Adamts4*<sup>em1Aduj</sup>

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## - Disease/Phenotype

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### + Disease Terms

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### + Research Areas By Phenotype

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### + Mammalian Phenotype Terms by Genotype

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### + References

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## Technical Support

### CONTACT TECHNICAL SUPPORT

#### Genotyping Protocols

End Point Analysis: [Trem2](#)

Probe: [App](#)

Probe: [Apoe-Probe](#)

[Genotyping resources and troubleshooting](#)

#### Breeding Considerations

When maintaining a live colony, mice homozygous for *Adamts4*<sup>em1Adiuj</sup> (Adamts4 enhancer KO), *Apoe*<sup>tm1.1(APOE\*4)Adiuj</sup> (APOE4), *App*<sup>em1Adiuj</sup> (hAbeta) and *Trem2*<sup>em1Adiuj</sup> (Trem2\*R47H) may be bred together as they are viable and fertile. [March 2020]

#### Additional Breeding and Husbandry Support

##### Mating System

Heterozygous for *Adamts4*<sup>em1Adiuj</sup> Homozygous for *Apoe*<sup>tm1.1(APOE\*4)Adiuj</sup> Homozygous for *App*<sup>em1Adiuj</sup>  
 Homozygous for *Trem2*<sup>em1Adiuj</sup> X Heterozygous for *Adamts4*<sup>em1Adiuj</sup> Homozygous for *Apoe*<sup>tm1.1(APOE\*4)Adiuj</sup>  
 Homozygous for *App*<sup>em1Adiuj</sup> Homozygous for *Trem2*<sup>em1Adiuj</sup>

#### Citation

When using the *Adamts4* enhancer KO/hAbeta/APOE4/*Trem2*\*R47H mouse strain in a publication, please [cite the originating article\(s\)](#) and include JAX stock #033868 in your Materials and Methods section.

## Pricing & Availability



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LIVE MOUSE			
AGE	SEX	GENOTYPE	PRICE
Approx 4-8 weeks	Female	Heterozygous for <i>Adamts4</i> <sup>em1Adiuj</sup> Homozygous for <i>Apoe</i> <sup>tm1.1(APOE*4)Adiuj</sup> Homozygous for <i>App</i> <sup>em1Adiuj</sup> Homozygous for <i>Trem2</i> <sup>em1Adiuj</sup>	\$255.00
	Male	Heterozygous for <i>Adamts4</i> <sup>em1Adiuj</sup> Homozygous for <i>Apoe</i> <sup>tm1.1(APOE*4)Adiuj</sup> Homozygous for <i>App</i> <sup>em1Adiuj</sup> Homozygous for <i>Trem2</i> <sup>em1Adiuj</sup>	\$255.00
Approx 4-8 weeks	Female	Homozygous for <i>Adamts4</i> <sup>em1Adiuj</sup> Homozygous for <i>Apoe</i> <sup>tm1.1(APOE*4)Adiuj</sup> Homozygous for <i>App</i> <sup>em1Adiuj</sup> Homozygous for <i>Trem2</i> <sup>em1Adiuj</sup>	\$255.00
	Male	Homozygous for <i>Adamts4</i> <sup>em1Adiuj</sup> Homozygous for <i>Apoe</i> <sup>tm1.1(APOE*4)Adiuj</sup> Homozygous for <i>App</i> <sup>em1Adiuj</sup> Homozygous for <i>Trem2</i> <sup>em1Adiuj</sup>	\$255.00

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