

B6.Cg-Pilra^{em1Aduj} **Apoe**^{tm1.1(APOE*4)Aduj} **App**^{em1Aduj} **Trem2**^{em1Aduj} /J
 Stock No: **032774** | Pilra^{G65R} /hAbeta/APOE4/Trem2*R47H

◆ Congenic, Endonuclease-Mediated Mutation, Targeted Mutation

Please contact Technical Support for more information

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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^{em1Aduj}

Alele Type	Gene Symbol	Gene Name
Endonuclease-mediated (Humanized sequence)	<i>Trem2</i>	triggering receptor expressed on myeloid cells 2

Apoe^{tm1.1(APOE*4)Aduj}

Alele Type	Gene Symbol	Gene Name
Targeted (Inserted expressed sequence, Humanized sequence)	<i>Apoe</i>	apolipoprotein E

App^{em1Aduj}

Alele Type	Gene Symbol	Gene Name
Endonuclease-mediated (Humanized sequence)	<i>App</i>	amyloid beta (A4) precursor protein

Pilra^{em1Adiuj}

Allele Type	Gene Symbol	Gene Name
Endonuclease-mediated (Not Specified)	<i>Pilra</i>	paired immunoglobulin-like type 2 receptor alpha

VIEW GENETICS

RESEARCH APPLICATIONS

Neurobiology Research
Mouse/Human Gene Homologs

VIEW ALL RESEARCH APPLICATIONS

Details

Detailed Description

Pilra^{G85R}/hAbeta/APOE4/Trem2*R47H quadruple mutant strain carries a mutant allele of the *Pilra* gene with amino acids at positions 85-88 edited from GEF1 to RQSF (modeling human SNP rs1859788), 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 *Pilra* gene encodes a cell surface inhibitory receptor, mutations of which have recently been shown to be protective against Alzheimer's disease. 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 *Pilra*^{em1Adiuj} (*Pilra* G85R SNP), *ApoE*^{tm1.1(APOE*4)Adiuj} (APOE4), *App*^{em1Adiuj} (hAbeta) and *Trem2*^{em1Adiuj} (Trem2*R47H) are viable and fertile [July 2020]. If additional characterization of these *Pilra*^{G85R}/hAbeta/APOE4/Trem2*R47H mice is performed, we may modify the strain description accordingly.

Of note, in brains of mice homozygous for the *Trem2*^{em1Adiuj} 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](#)).

Development

[+ Expression Data](#)

[+ Control Suggestions](#)

[- Genetics](#)

[+ *Trem2*^{em1Aduj}](#)

[+ *ApoE*^{tm1.1\(APOE*4\)Aduj}](#)

[+ *App*^{em1Aduj}](#)

[+ *Pilra*^{em1Aduj}](#)

[- Disease/Phenotype](#)

[+ Disease Terms](#)

[+ Research Areas By Phenotype](#)

[+ Mammalian Phenotype Terms by Genotype](#)

[+ References](#)

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C O N T A C T T E C H N I C A L S U P P O R T

Genotyping Protocols

[Genotyping resources and troubleshooting](#)

Breeding Considerations

When maintaining a live colony, mice homozygous for *Pilra*^{em1Aduj} (*Pilra*^{G85R}), *ApoE*^{tm1.1(APOE*4)Aduj} (APOE4), *App*^{em1Aduj} (hAbeta) and *Trem2*^{em1Aduj} (Trem2*R47H) may be bred together as they are viable and fertile. [July 2020]

[Additional Breeding and Husbandry Support](#)

Citation

When using the Pilra^{G85R}/hAbeta/APOE4/Trem2*R47H mouse strain in a publication, please [cite the originating article\(s\)](#) and include JAX stock #032774 in your Materials and Methods section.

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