

B6.Cg-Apoe^{tm1.1(APOE*4)AdiuJ} Il1rap^{em2AdiuJ} App^{em1AdiuJ} Trem2^{em1AdiuJ} /J

Stock No: **032777** | Il1rap^{ex3KO} /hAbeta/APOE4/Trem2*R47H

◆ Congenic, Endonuclease-Mediated Mutation, Targeted Mutation

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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^{em1AdiuJ}

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)AdiuJ}*

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

App^{em1AdiuJ}

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

Alele Type	Gene Symbol	Gene Name
Endonuclease-mediated (Null/Knockout)	<i>Il1rap</i>	interleukin 1 receptor accessory protein

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RESEARCH APPLICATIONS

Neurobiology Research
Mouse/Human Gene Homologs

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Details

Detailed Description

Il1rap^{ex3KO}/hAβeta/APOE4/Trem2*R47H quadruple mutant strain carries a mutant allele of the *Il1rap* lacking exon 3 (modeling human intronic variant rs12053868), 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 *Il1rap* gene encodes a component of the interleukin 1 receptor complex, which initiates signaling events that result in the activation of interleukin 1-responsive genes. The encoded gene has also been associated with amyloid accumulation in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort. 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 *Il1rap*^{em2Aduj} (*Il1rap*^{ex3KO}), *ApoE*^{tm1.1(APOE*4)Aduj} (APOE4), *App*^{em1Aduj} (hAβeta) and *Trem2*^{em1Aduj} (Trem2*R47H) are viable and fertile [July 2020]. If additional characterization of these *Il1rap*^{ex3KO}/hAβeta/APOE4/Trem2*R47H mice is performed, we may modify the strain description accordingly.

Of note, in brains of mice homozygous for the *Trem2*^{em1Aduj} 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](#)

[- Genetics](#)

[+ Trem2^{em1Aduj}](#)

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

[+ App^{em1Aduj}](#)

[+ Il1rap^{em2Aduj}](#)

[- 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 *Apoe*^{tm1.1(APOE*4)Aduj} (APOE4), *Il1rap*^{em2Aduj} (*Il1rap*^{ex3KO}), *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 Il1rap^{ex3KO}/hAbeta/APOE4/Trem2*R47H mouse strain in a publication, please [cite the originating article\(s\)](#) and include JAX stock #032777 in your Materials and Methods section.

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