These 5XFAD transgenic mice overexpress mutant human amyloid beta (A4) precursor protein 695 (APP) with the Swedish (K670N, M671L), Florida (I716V), and London (V717I) Familial Alzheimer’s Disease (FAD) mutations along with human presenilin 1 (PS1) harboring two FAD mutations, M146L and L286V. Both transgenes are regulated by the mouse Thy1 promoter to drive overexpression in the brain. 5XFAD mice recapitulate major features of Alzheimer’s Disease amyloid pathology and may be a useful model of intraneuronal Abeta-42 induced neurodegeneration and amyloid plaque formation.

Donating Investigator

Robert Vassar, Northwestern University
These 5XFAD transgenic mice overexpress both mutant human amyloid beta (A4) precursor protein 695 (APP) with the Swedish (K670N, M671L), Florida (I716V), and London (V717I) Familial Alzheimer's Disease (FAD) mutations and human presenilin 1 (PS1) harboring two FAD mutations, M146L and L286V. Expression of both transgenes is regulated by neural-specific elements of the mouse Thy1 promoter to drive overexpression in the brain. Mice from this 6799 founder line have high APP expression correlating with high burden and accelerated accumulation of the 42 amino acid species of beta-amyloid (Abeta-42). 5XFAD mice generate Abeta-42 almost exclusively, rapidly accumulating massive cerebral levels. On this mixed C57BL/6 and SJL background (MMRRC stock 34840), intraneuronal Abeta-42 accumulation is observed starting at 1.5 months of age, just prior to amyloid deposition and gliosis, which begins at two months of age. On a congenic C57BL/6J genetic background (see MMRRC stock 34848) it has been the observation of the MMRRC that this phenotype is not as robust as that demonstrated in the mixed C57BL/6 and SJL background (view data). In addition, these mice have reduced synaptic marker protein levels, increased p25 (formally Cdk5) levels, neuron loss, reduced anxiety, poor novel object recognition, impaired conditioned behavior and memory impairment in the Y-maze test. 5XFAD transgenic mice recapitulate major features of Alzheimer's Disease amyloid pathology and may be useful models of intraneuronal Abeta-42 induced neurodegeneration and amyloid plaque formation. Hemizygous mice are viable and fertile.

This strain is segregating heterozygous/wild type for the retinal degeneration allele Pde6b<sup>rd1</sup>. It should be noted that the SJL genetic background contains the Trem2<sup>S148E</sup> allele - a naturally occurring variant at position 48351151-48351152 on Chr 17 (rs108080490 and rs107649577; Ensembl GRCm38.p6). This TC to GA transition results in a serine to glutamic acid substitution at amino acid 148 (S148E). Because this model (MMRRC stock 34840) is maintained by backcrossing transgenic animals to a B6SJLF1 hybrid at every generation, SJL content is segregating in the progeny of these animals. Mice produced from this cross could be genotypically heterozygous, homozygous or wildtype for this Trem2<sup>S148E</sup>. This variant may be of particular interest to those studying the role played by TREM2 (triggering receptor expressed on myeloid cells 2) in Alzheimer's Disease pathology.

NOTE: This 5XFAD transgene is also available on a C57BL/6J background (see MMRRC stock 34848), which does not carry the Trem2<sup>S148E</sup> allele.
Genotyping Protocols
Standard PCR: Generic Pde6b
Standard PCR: Generic Pde6b Alternate1
Probe: Pde6b Probe
Standard PCR: Tg(APPSwFlOn,PSEN1*M146L*L286V)6799Vas-Chr3
Sanger sequencing: Trem2 rs107649577-SEQ

Genotyping resources and troubleshooting

Dietary Information
LabDiet® 5K52 formulation (6% fat)

Breeding Considerations
When maintaining a live colony, hemizygous mice may be bred to B6SJLF1/J (Stock No. 100012).

Additional Breeding and Husbandry Support
Mating System
Hemizygote x F1
F1 x Hemizygote
Appearance
multiple coat colors
Related Genotype: segregating for a, A, Oca2O, Tyr and Pde6b

c1

Citation
When using the 5XFAD mouse strain in a publication, please cite the originating article(s) and include MMRRC stock #34840 in your Materials and Methods section.

Animal Health Reports
Facility Barrier Level Descriptions
- AX10 (Standard)

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