Overview

Also Known As: A-R1.40

These R1.40 transgenic mice express all mRNA and protein isoforms of the human amyloid beta (A4) precursor protein \( \text{APP} \) containing the Familial Alzheimer's Disease (FAD) Swedish mutation K670N/M671L, and may be useful in studying the pathogenesis of Familial Alzheimer's Disease and possible therapeutic treatments.

Donating Investigator

Bruce Lamb, Indiana University School of Medicine
These R1.40 transgenic mice express all mRNA and protein isoforms of the human amyloid beta (A4) precursor protein \( \text{APP} \) containing the Familial Alzheimer's Disease (FAD) Swedish mutation K670N/M671L. Transgene expression (mRNA and full-length protein) is 2 to 3 fold the endogenous mouse \( \text{App} \) expression level in the hemizygous state in brain tissue as revealed by RT-PCR and Western Blot analysis. Transgene expression pattern mimics endogenous mouse gene expression patterns. The donating investigator reports increased mortality in young homozygous animals (higher incidence in females). 3 to 4 month old transgenic mice, maintained on a C57BL/6J background, exhibit spontaneous seizure-like events (abnormal spiking) in EEG readings, without abnormal behavior and are more susceptible to kainic acid induced seizures (Vogt et al. Neurobiol Aging 2009). These R1.40 transgenic mice may be useful in studying the pathogenesis of Familial Alzheimer's Disease and possible therapeutic treatments.

In an attempt to offer alleles on well-characterized or multiple genetic backgrounds, alleles are frequently moved to a genetic background different from that on which an allele was first characterized. It should be noted that the phenotype could vary from that originally described. A publication (Lehman et al. 2003 Hum Mol Genet 12:2949) compares the well characterized B6-R1.40 strain (B6.129-Tg(APPSw40Btla/Mmjax) with two additional congenic strains, D2-R1.40 (D2.129(B6)-Tg(APPSw40Btla/Mmjax) and 129S1-R1.40 (129S1.129(Cg)-Tg(APPSw40Btla/Mmjax). While these three congenic strains have similar levels of holo-\( \text{APP} \) in brain tissue, the levels of brain \( \text{APP} \) C-terminal fragments (CTFs) vary depending upon genetic background. Brain and plasma levels of amyloid beta-40 and -42 are variable as well (B6-R1.40 > 129S1-R1.40 > D2-R1.40). In addition, the congenic strains exhibited dramatic alterations in the age of onset of amyloid beta deposition; in contrast to 14 month old homozygous B6-R1.40 mice, homozygous D2-R1.40 and 129S1-R1.40 mice do not develop amyloid beta deposits in the parietal or frontal cortex even by 20 months of age. The donating investigator further reports that the A-R1.40 strain (A.129(B6)-Tg(APPSw40Btla/Mmjax) exhibits levels of amyloid beta comparable to the B6-R1.40 strain, but with later onset. Therefore, APP processing and amyloid beta metabolism and deposition are modified by the genetic background. While the 129S1-R1.40 strain can be easily maintained as homozygotes, the donating investigator reports increased mortality in young homozygotes on the other genetic backgrounds, with D2-R1.40 and A-R1.40 more severely affected than B6-R1.40.
Genotyping Protocols
QPCR: Generic APP human genomic or cDNA
Standard PCR: Tg(APPSw)40Btla
Standard PCR: Generic APP MCA human genomic
Probe: Generic APP human genomic or cDNA
Genotyping resources and troubleshooting

Breeding Considerations
When maintaining a live colony, transgenic carriers may be bred together, to wildtype siblings, or to A/J inbred mice. Because of the increased mortality in young homozygous animals (higher incidence in females), maintaining the colony by breeding homozygotes together is only recommended when sufficient colony size is permitted.

Additional Breeding and Husbandry Support

Citation
When using the A.129(B6)-Tg(APPSw)40Btla/Mmjax mouse strain in a publication, please cite the originating article(s) and include MMRRC stock #34841 in your Materials and Methods section.

Animal Health Reports
Production of mice from cryopreserved embryos or sperm occurs in a maximum barrier room, G200

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