Overview

R E A D  M O R E  +

Also Known As: APP/PS1

APP/PS1 are double transgenic mice expressing a chimeric mouse/human amyloid precursor protein (Mo/HuAPP695swe) and a mutant human presenilin 1 (PS1-dE9), both directed to CNS neurons. Both mutations are associated with early-onset Alzheimer's disease. These mice may be useful in studying neurological disorders of the brain, specifically Alzheimer's disease, amyloid plaque formation and aging.

Donating Investigator

Dr. David R Borchelt, University of Florida
APP/PS1 are double transgenic mice expressing a chimeric mouse/human amyloid precursor protein (Mo/HuAPP695swe) and a mutant human presenilin 1 (PS1-dE9), both directed to CNS neurons. Both mutations are associated with early-onset Alzheimer's disease. The "humanized" Mo/HuAPP695swe transgene allows the mice to secrete a human A-beta peptide. Both the transgenic peptide and holoprotein can be detected by antibodies specific for human sequence within this region (Signet Laboratories' monoclonal 6E10 antibody). The included Swedish mutations (K595N/M596L) elevate the amount of A-beta produced from the transgene by favoring processing through the beta-secretase pathway. This "humanized" Mo/HuAPP695swe protein is immunodetected in whole brain protein homogenates. The transgenic mutant human presenilin protein (PS1-dE9), which in high levels displaces detectable endogenous mouse protein, is also immunodetected in whole brain protein homogenates. The donating investigator reports that transgenic mice develop beta-amyloid deposits in brain by 6 to 7 months of age. Between 6 and 15 months of age, mice exhibit a gender-based disparity in beta-amyloid burden. Females develop a 5-fold ($A\beta_{42}$) and 10-fold ($A\beta_{40}$) increase in beta-amyloid deposits in the cerebellum by 15 months as compared to males. Accumulation of plaques is more abundant in the molecular layer than in the granular layer. In the cortex, the beta-amyloid burden is increased in both sexes in parallel (Ordonez-Gutierrez et al. Jnl Alz Dis 2016).

APP/PS1 hemizygotes on a C57BL/6J-congenic background (Stock No. 005864) exhibit seizure activity. Specifically, hemizygous mice on the C57BL/6 background (N9B6) exhibit a high incidence of seizures, as detected by video-EEG. 25% of transgenic mice, 3 to 3.5 months in age, exhibit at least 1 seizure. By 4.5 months of age, seizure incidence increases to 55%. In mice with seizures a 10-15% mortality is reported on the congenic (N9) C57BL/6 background. In these mice, sudden deaths occur at any age but peak around 3-4 months (Minkeviciene et al. J Neurosci. 2009). At 17-18 weeks of age, hemizygous mice on the congenic C57BL/6J background (N13) exhibit epileptiform discharges as detected by video-EEG. Mortality was 38% (6/16) and some mutant mice experienced spontaneous seizures during the experiments. Antiepileptic drugs (carbamazepine, phenytoin, valproate) reduce the frequency of spontaneous electrographic epileptiform discharges (Ziyatdinova et al. Epilepsy Res 2011).

In contrast, APP/PS1 hemizygotes on a C57BL/6;C3H genetic background (see Stock No. 004462) do not exhibit any seizure phenotype.

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. This is the case for the C57BL/6J-congenic background (Stock No. 005864). It should be noted that the phenotype could vary from that originally described. We will modify the strain description if necessary as published results become available.
Genotyping Protocols
Probe: Generic APP Version 2 Probe
Standard PCR: Tg(PSEN1)
Standard PCR: Generic Tg(APP)
Standard PCR: Generic Human PSEN1 cDNA Multiplex1
Standard PCR: Tg(PSEN1)
Standard PCR: Tg(APPswe,PSEN1dE9)85Dbo-Chr9
Probe: Tg(APPswe,PSEN1dE9)85Dbo-Chr9 Probe
Separated PCR: Meox2cre
Probe: Mapt-Probe
Genotyping resources and troubleshooting

Breeding Considerations
When maintaining a live colony, C57BL/6J females are bred to hemizygous male mice. Hemizygous females and males appear to die prematurely. While the donating investigator indicates aggressive behavior has been observed (particularly for transgenic males) and transgenic females can exhibit suboptimal mothering of litters, no such complications have been observed in our colonies at The Jackson Laboratory.

Additional Breeding and Husbandry Support
Mating System
C57BL/6J (000664) x Hemizygote

Citation
When using the APP/PS1 mouse strain in a publication, please cite the originating article(s) and include MMRRC stock #34832 in your Materials and Methods section.

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

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