B6C3-Tg(APPswe,PSEN1dE9)85Db/Mmjax

MMRRC Stock No: 34829-JAX | APP/PS1

Transgenic

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Live mice available in varying quantities. Ask Customer Service for details.
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

GENETIC OVERVIEW
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<th>Genetic Background</th>
<th>Generation</th>
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Tg(APPswe,PSEN1dE9)85Db

Allele Type
Transgenic (Insert expressed sequence, Humanized sequence)

RESEARCH APPLICATIONS
Neurobiology Research
Mouse/Human Gene Homologs
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 (K597N/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\textsubscript{42}) and 10-fold (A\textsubscript{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/6C3H genetic background (Stock No. 004462) do not exhibit any seizure phenotype. These animals also display a slight alteration in their tail phenotype (e.g., kinked tail) that is believed to be due to the mixed genetic background of the strain and is not related to transgene expression. This strain does not carry the retinal degeneration allele Pde6b\textsuperscript{rd1}.

In contrast, APP/PS1 hemizygotes on a C57BL/6J-congenic background (see Stock No. 005864) exhibit seizure activity. Specifically, hemizygous mice on the C57BL/6 background (N986) 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%. 10-15% mortality is reported for transgenic mice on the congenic (N9) C57BL/6 background (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).
Genotyping Protocols
QPCR: Generic Human PSEN1 cDNA Probe
Genotyping resources and troubleshooting

Breeding Considerations
When maintaining a live colony, hemizygotes may be bred with wildtype (noncarrier) siblings. Coat color expected from breeding is black or agouti. While the donating investigator warns that male aggression may require individual housing, there are no such reports of this problem in our colonies at The Jackson Laboratory to date (June 2006).

Additional Breeding and Husbandry Support

Mating System
+/+ sibling x Hemizygote

Citation

When using the APPIC1 mouse strain in a publication, please cite the originating article(s) and include MMRRC stock #34829 in your Materials and Methods section.

Animal Health Reports
Facility Barrier Level Descriptions

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