Overview

Also Known As: Prp-TDP43\textsuperscript{A315T}

Prp-TDP43\textsuperscript{A315T} transgenic mice express a mutant human TAR DNA binding protein cDNA harboring an amino acid substitution associated with familial ALS. Hemizygous mice develop a progressive and fatal neurodegenerative disease reminiscent of both ALS and frontotemporal lobar degeneration with ubiquitin aggregates. These transgenic mice may be useful in studying...
neuromuscular and neurodegenerative disorders such as ALS (Lou Gehrig’s Disease) and frontotemporal lobar degeneration with ubiquitin aggregates.

Our preclinical efficacy testing services offer scientific expertise and an array of target-based and phenotype-based outcome measures, both in vivo and at endpoint, for flexible study designs and assay development in mouse models of Amyotrophic Lateral Sclerosis. See our full service platform.

Donating Investigator
Robert H Baloh, Cedars Sinai Medical Center

GENETIC OVERVIEW

<table>
<thead>
<tr>
<th>Genetic Background</th>
<th>Generation</th>
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<tr>
<td></td>
<td>N5+N13</td>
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**Tg(Prnp-TARDBP*A315T)95Balo**

**Allele Type**
Transgenic (Inserted expressed sequence, Humanized sequence)

RESEARCH APPLICATIONS

Neurobiology Research
Mouse/Human Gene Homologs

BASE PRICE
Starting at:
$255.00 Domestic price for female 4-week

Mice hemizygous for this Prp-TDP43^{A315T} transgene are viable, fertile, and express a mutant human TAR DNA binding protein (*TARDBP* or TDP-43) cDNA harboring an N-terminal Flag tag and an A315T amino acid substitution that is associated with familial Amyotrophic Lateral Sclerosis (ALS). Expression is directed throughout the nervous system by mouse prion protein (*PrP* or *Pmp*).
Hemizygous mice were originally published on a mixed C57BL/6;CBA genetic background and develop a progressive gait disorder around 3-4 months of age with death around 5 months of age. For hemizygous mice on a mixed C57BL/6;CBA genetic background, the donating investigator reports that, on average, males die almost one month earlier than females. Due to continued backcrossing to C57BL/6J at The Jackson Laboratory Repository, this strain is now fully congenic on a C57BL/6J background. Survival differences between male and female hemizygous mice are still observed. However, hemizygous males on a C57BL/6J genetic background have an average survival time of approximately 3.5 months (97 +/- 11 days); this is earlier lethality than hemizygous males on a mixed C57BL/6;CBA genetic background. On a C57BL/6J genetic background, hemizygous females live significantly longer than hemizygous males. In addition, male mice exhibit a progressive neurodegeneration in the myenteric plexus of the colon, which is characterized by reduced GI motility and contributes to the decreased lifespan observed in these mice. This phenotype is most severe in males on the C57BL/6J background. For more detailed information, please view graph of B6.Tg(Prnp-TARDBP*A315T)95Balo/J survival and data 2010-2012. [pdf] The intestinal dysmotility phenotype observed in these mice can be mitigated by the use of jellified food. Mice fed jellified food survive and develop a progressive motor phenotype including gait abnormalities, denervated neuromuscular junctions, gastrocnemius muscle atrophy, and upper and lower motor axon loss (especially large axons). (Herdewyn et. al. Mol Neuro 9:24, 2014)

The progressive and fatal neurodegenerative disease phenotype of hemizygous mice is reminiscent of both ALS and frontotemporal lobar degeneration with ubiquitin aggregates (FTLD-U). Specifically, hemizygous mice accumulate pathologic aggregates of ubiquitinated proteins only in specific neuronal populations, including frontal cortex layer V pyramidal neurons and spinal motor neurons with activation of local astrocytes and microglia. Loss of both upper and lower motor neurons is also observed. TDP-43 aggregates are not reported in the cytoplasm. The donating investigator has not attempted to make homozygous mice.

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. As the Prp-TDP43\textsuperscript{A315T} transgenic mice were originally created on a mixed C57BL/6;CBA genetic background, it should be noted that the phenotype of these Prp-TDP43\textsuperscript{A315T} transgenic mice on a C57BL/6-congenic background may vary greatly from that originally described. We will modify the strain description if necessary as published results become available.
Genotyping Protocols
Standard PCR: Tg(Prnp-TARDBP*A315T)95Balo
Standard PCR: Tg(Prnp-TARDBP*A315T)95Balo
QPCR: Tg(Prnp-TARDBP*A315T)95Balo

Genotyping resources and troubleshooting

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

Breeding Considerations
When maintaining a live colony, hemizygous carriers may be bred with wildtype (noncarrier) mice from the colony or C57BL/6J
inbred mice (Stock No. 000664). Hemizygous males on a C57BL/6J genetic background have an average survival time of
approximately 3.5 months (97 +/- 11 days); this is earlier lethality than hemizygous males on a mixed C57BL/6;CBA genetic
background. On a C57BL/6J genetic background, hemizygous females live significantly longer than hemizygous males. The intestinal
dysmotility phenotype and sudden death observed in these mice can be mitigated by the use of jellified food. (Herdewyn et. al. Mol
Neuro 9:24, 2014)
The donating investigator has not attempted to make homozygous mice.

Additional Breeding and Husbandry Support

Mating System
Hemizygote x Noncarrier
Noncarrier x Hemizygote

Citation
When using the Prp-TDP43A315T mouse strain in a publication, please cite the originating article(s) and include JAX stock #010700
in your Materials and Methods section.

Pricing & Availability
Available Now

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

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<th>AGE</th>
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<th>PRICE</th>
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Related Strains

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