Tremor and reduced lifespan 2 Jackson: a new remutation on Chromosome 10.

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Mutation (allele) symbol: *Hcn2*$^{trls\text{-}2J}$

Mutation (allele) name: tremor and reduced lifespan 2 Jackson

Gene symbol: *Hcn2* (updated September 2012)

Strain of origin: WB/ReJ-*Kit*^{W}/J

Current strain name: B6.WB-*Hcn2*$^{trls\text{-}2J}$/J

Stock #008723 (jaxmice.jax.org)

Phenotype categories: neurological

Abstract

A new neurological mutation has been identified and characterized as a remutation of tremor and reduced lifespan (*trls*), as shown by a direct test for allelism. The new mutation was named tremor and reduced lifespan 2 Jackson (*trls*^{2J}).

Origin and Description

This new spontaneous mutation arose in a breeding colony of WB/ReJ-*Kit*^{W}/J mice at the Jackson Laboratory and was discovered by Jessica Rau. Mice homozygous for the *trls*^{2J} mutation can be recognized at about 14 days of age by a moderate tremor and smaller body size than their littermates. Progressive weakness and wasting follows, and death occurs by 3-4 weeks of age, but mutants seldom live longer than 4 weeks. The description of the original *trls* mice states that mutant mice are rarely able to survive to 10 weeks of age.

The *trls*^{2J} colony is maintained by breeding hosts of homozygous ovarian transplants to C57BL/6J mice and than intercrossing the heterozygous offspring. These matings were continued for four backcross generations to C57BL/6J without seeing any mice with the *Kit*^{W} (diluted black with white belly spot) phenotype. Heterozygous (*trls*^{2J}/+) mice can live normal life spans and are good breeders.

Genetic Analysis

A mouse homozygous for the *trls*^{2J} mutation was mated to a CAST/EiJ mouse. The F1 mice from this mating produced a normal looking phenotype, proving that this mutation has recessive inheritance.

Based on phenotypic similarities, a direct test for allelism was performed by mating WB/ReJ-*Kit*^{W}/J mice carrying this new mutation to BKS(Cg)-*trls*/J mice (+/*trls*). Three mating pairs were set up that produced 40 progeny, of which 13 pups had the *trls* mutant phenotype, proving allelism.

The original *trls* mutation was mapped to Chromosome 10 between *D10Mit115* (NCBIm 34 position 70.3 Mb) and *D10Mit65* (NCBIm 34 position 84.1 Mb) and is non-recombinant with *D10Mit7* (NCBIm 34 position 81.2Mb) and *D10Mit42* (NCBIm 34 position 82.5 Mb).

Pathology

A routine pathological examination of one homozygous mouse at 5 weeks of age showed testicular atrophy and two homozygous mice at 3 weeks of age had atrophic thymuses.

The eyes of one mutant mouse at age 4 weeks were tested by electroretinogram (ERG) and found to be normal.

Hearing as assessed by auditory-evoked brainstem response testing of two mutant mice at 4 weeks of age and one mutant mouse at 3 weeks of age showed normal thresholds, but there were noticeable peaks with long latencies, which may indicate deficient myelin.

Acknowledgements

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Update

In 2012 it was found that *trls* is a mutation in *Hcn2* and by inference so is the *trls*^{2J} mutation.