

A Second Allele of Tremor With Tilted Head

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Mutation (allele symbol): *tth*^{2J}

Mutation (allele) name: tremor with tilted head 2 Jackson

Current strain name: B6.NOD-*tth*^{2J}/KjnJ

Stock #012306 (jaxmice.jax.org)

Phenotype categories: neurological/behavioral

Abstract

A recessive mutation causing a tilted head, tremor, circling, and failed swim test (but not significant hearing loss) arose spontaneously on a predominantly NOD background. This mutation was mapped to distal Chromosome 15 and a failed complementation test with the original tremor with tilted head mutant (*tth*) proved them to be alleles.

Origin and Description

In 2004 a spontaneous mutation was discovered in an NOD transgenic strain in the laboratory of Dr. David Serreze at The Jackson Laboratory. Mutants display a head tilt phenotype, a tremor when walking, and some display circling behavior. The phenotype is visible by 4 weeks of age. Auditory brainstem response analysis (ABR) revealed severe hearing loss in both mutants and control siblings due to the NOD background, but when this new mutation was bred onto a C57BL/6J background, the severe hearing loss was not found and so is not attributable to the mutation. Homozygotes on this C57BL/6J congenic background are unable to orient to swim at the surface of water but instead swim underwater and require rescue.

Genetic Analysis

This new mutation was mapped to distal Chromosome 15 using the standard mapping protocol of The Mouse Mutant Resource. Of twenty F2 mutants assessed, marker *D15Mit42* had only 1 recombinant, and marker *D15Mit44* had none. Due to this map location and the similarity in phenotype with the mutant tremor with tilted head (*tth*), an allele test was established. One female heterozygous for the new mutation was bred with a male heterozygous for *tth*, and the first litter had 7 pups of which 3 were missing at the time of phenotypic assessment and one was a mutant showing the head tilt phenotype.

Thus, this new mutation has been designated tremor with tilted head 2 Jackson, *tth*^{2J}. To date, efforts to sequence the genetic lesion for the tremor with tilted head mutations have not yielded any candidate mutations.

Acknowledgments

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