Quivering 10 Jackson and quivering 11 Jackson; two new remutations in the *Spnb4* gene.

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Mutation (allele) symbols: *qv-10J*; *qv-11J*

Mutation (allele) names: quivering 10 Jackson; quivering 11 Jackson

Gene symbol: *Spnb4*

Strains of origin: C;B6 (*qv-10J*) and C57BL/6J (*qv-11J*)

Current strain names: C;B6/-*Spnb4*$^{qv\text{-}10J}$/GrsrJ; C57Bl/6J-*Spnb4*$^{qv\text{-}11J}$

Stock #: 008521 (*qv-10J*); 008522 (*qv-11J*) (jaxmice.jax.org)

Phenotype categories: neurological

Abstract
We have identified two new recessive remutations in the *Spnb4* gene, *qv-10J* and *qv-11J*. Mice affected by these mutations have similar neurological phenotypes, including body tremor. For *qv-10J*, a direct test for allelism was performed and confirmed with the previously described quivering mutation (*Spnb4*^{qv}), while allelism for *qv-11J* was proven by testing with *qv-10J*.

Origin and Description
The quivering 10 Jackson remutation was found at The Jackson Laboratory in the progeny of a BALB/cJ-*ichq* X C57BL/6J mating. Mice affected by the *qv-10J* mutation can be recognized by two months of age by a mild wobble and tremors in the hind end. This phenotype progressively worsens with age. The quivering 10 Jackson mutation has been maintained by a brother X sister mating scheme. Either homozygote female x heterozygous male matings or heterozygote x heterozygote matings (in either direction) are utilized. This mutation has been found to originate in the BALB/cJ parent. Unlike the original *qv* mutants that die at 5 months of age, most *qv-10J* mutants live a normal lifespan. Males carrying the *qv-10J* mutation appear to be sterile, but females do breed.

The quivering 11 Jackson remutation was identified by Marcus Boland in a C57BL/6J production colony. The mutant phenotype is visible by three weeks of age and includes a body tremor and an abnormal hind leg gait. The male mutant mice do not breed, so the quivering 11 Jackson colony is maintained by breeding a homozygous female to a heterozygous male. Quivering 11 Jackson mice appear to live a normal lifespan.

Genetic Analysis

Evidence for allelism: Two female mice homozygous for the quivering 10J mutation were mated to a heterozygote C3H/HeJ-*qv*$^{lnd\text{-}2J}$/+ male mouse. This mating produced seven affected mice out of a total of 26 born proving allelism. Using standard mapping protocols some of the affected mice were confirmed by mapping to be in the same location (28.1-28.2 Mb) as the original quivering mutation on Chromosome 7. A female mouse homozygous for the quivering 10J mutation was mated to a heterozygous quivering 11 J male. This mating produced three litters totaling 14 mice, of which 8 were mutant, thus confirming allelism.

Pathology

A routine pathological screen of 3 *qv-10J* mutants at 5 weeks of age, 1 at 6 weeks of age and two at 7 weeks of age showed no gross abnormalities, similar to the pathology of the original quivering mutation. The eyes of five mutants and two controls at five weeks of age were examined with an ophthalmoscope and were determined to be normal normal. Hearing as assessed by auditory brainstem response (ABR) testing for both mutations revealed hearing impairment. Five *qv-10J* mutants at five weeks of age displayed severe hearing loss with no ABR detected at the highest intensities tested (100 dB SPL), while two controls at five weeks of age had normal hearing. Three *qv-11J* mutant mice were assessed for hearing between four and fourteen weeks. These mice displayed only slightly elevated hearing thresholds indicating hearing impairment, but not deafness. Interestingly, the ABR wave-form pattern for each mutation was different (Fig 1). Quivering 10 Jackson mice produced a wave pattern similar to the originally described quivering mutation (*qv*), consisting of only the first ABR peak, while quivering 11 Jackson mice produced a less aberrant pattern, indicating that the demyelination caused by the *qv-11J* mutation is probably not as severe as that of *qv* and *qv-10J*. The quivering 11 Jackson allele retains all five peaks associated with a normal ABR click response (see figure below), however, a decrease in amplitude and increase in latency is observable in the *qv-11J* traces when compared to the control.

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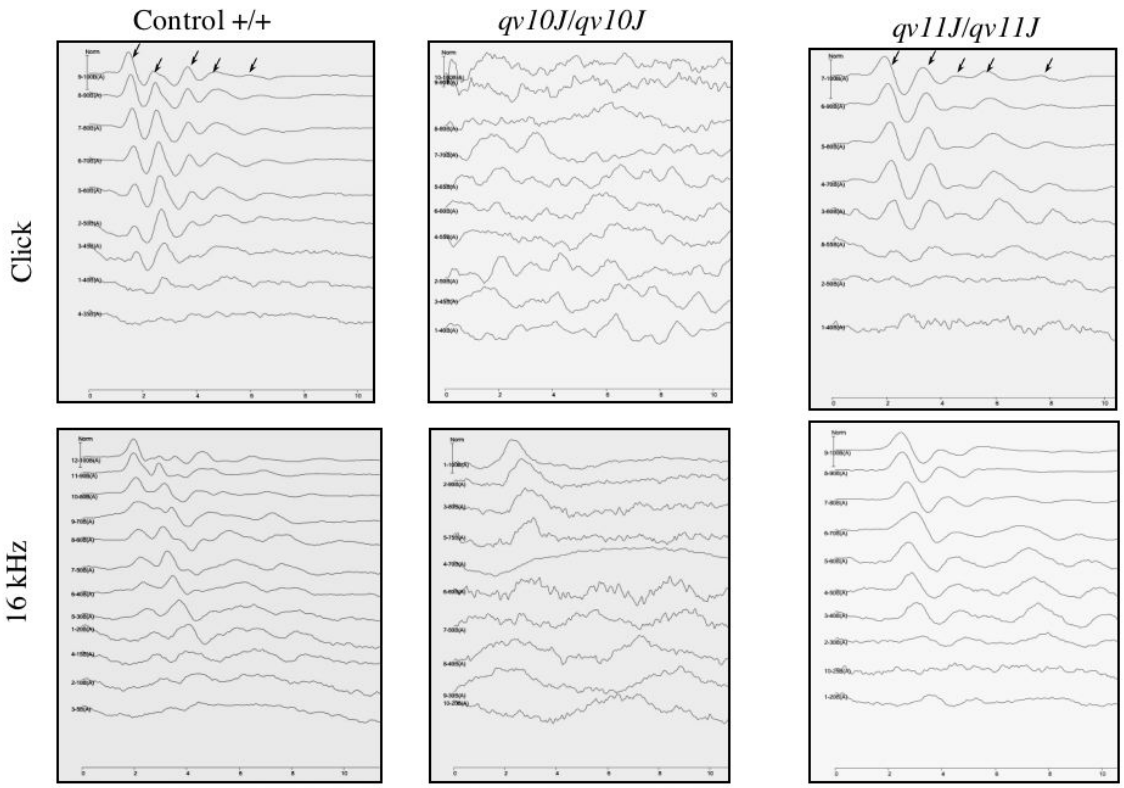

ABR traces of a control +/+, *qv-10J* mutant and *qv-11J* mutant mice. All traces show a normalized instead of a fixed scale. An increase in latency of the ABR click response is observable in the *qv-11J* allele while the overall response is reduced at 16 kHz.