A Neurological Mutation on Chromosome 14 named shimmy 3 Jackson

Patricia Ward-Bailey, Richard Samples, Jill Giggey, Leah Rae Donahue, Roderick Bronson, Muriel Davisson

Source of Support: This research was supported by grants RR01183 to the Mouse Mutant Resource (M.T. Davisson, PI) and Cancer Core Grant CA34196.

Mutation (allele) symbol: *shmy*^{3J}

Mutation (allele) name: shimmy 3 Jackson

Strain of origin: C3.MRL-*Fas*^{lpr}/J

Current strain name: STOCK-*Fas*^{lpr}-*shmy*^{3J}/GrsrJ

Stock #005132 (jaxmice.jax.org)

Phenotype categories: neurological

Abstract
A neurological mutation exhibiting a shaky/wobbly gait has been identified and mapped to Chromosome 14 in the same region as the mutation shimmy (*shmy*). A complementation test for allelism between this new mutant and the B10.D1-*H2*^{q}/SqJ-*shmy*^{2J}/J mutant produced affected animals proving that they are allelic.

Origin and Description
Mice carrying the spontaneous recessive *shmy*^{3J} mutation were found by Susan Swana in August 2001 in a production colony of C3.MRL-*Fas*^{lpr}/J mice (Stock #000480) at The Jackson Laboratory and were brought to The Mouse Mutant Resource (MMR). Homozygous mutants are easily recognized by 3 weeks of age by their shaking and wobbly gait. The parents of the *shmy*^{3J} mice brought to the MMR had tumors and died before producing more litters. Two affected males from the original litter were mated to C57BL/6J to continue this mutation. As of this date (10-14 -04) the new strain has been mated to C57BL/6J for two generations.

Genetic Analysis
Using the standard mapping protocols of The Mouse Mutant Resource, an intercross between C3H.MRL-*Fas*^{lpr}-*shmy*^{3J}/J and CAST/Ei F1 hybrids was set up and generated 60 affected F2 animals for linkage analysis. The *shmy*^{3J} mutation maps to mouse Chromosome 14, distal to *D14Mit207* (at 5.5 cM) and proximal to *D14Mit253* (at 7.5cM). The previously described mutation shimmy (*shmy*) has been mapped to position 6.5 cM. A direct test for allelism was set up by mating a mouse homozygous for this new mutation with a mouse heterozygous for the *shmy-2J* mutation. From this mating 3 progeny out of 4 born were affected proving that the new mutation is an allele of shimmy.

Pathology

A pathological screen of two *shmy*^{3J}/*shmy*^{3J} mutants aged 3.5 and 10 months of age revealed no brain lesions. In one mutant a few muscle fibers had abnormal banding, but not enough to cause the shaky gait. The other mutant had retinal degeneration and lymphoid hyperplasia, both characteristic of the C3.MRL-*Fas*^{lpr}/J background strain (the retinal degeneration characteristic of C3H and the lymphoid hyperplasia characteristic of MRL). The pathological studies of the original *shmy* mice showed a very few dystrophic axons in the lateral nucleus of the cerebellum in mutants, but did not reveal the cause of the neurological phenotype (Lane, et al. 1994).

Hearing of two homozygotes and one heterozygote as assessed by ABR testing was determined to be normal.

Discussion

The similarity in neurological phenotype, chromosomal location and the results of the test for allelism confirm that *shmy*^{3J} is a remutation to shimmy (*shmy*). Likewise, the chromosomal location of *shmy*^{3J} and it's locomoter phenotypes, which are similar to BK Channel (BK-/-) knockout mice (Sausbier, et al.2004) make the *Kcnma1* gene a good candidate for the *shmy* mutation.

Acknowledgements

The authors wish to thank Coleen Marden for excellent technical skills and Heping Yu for ABR testing.

References

Lane PW, Cook SA, Bronson RT, Johnson KR, and Davisson MT. SHIMMY (*shmy*), A New Mutation On Chromosome 14 Of The Mouse. Mouse Genome 1994, 92(4), 686-687.

Mouse Genome Database (MGD) Mouse Genome Informatics Project, The Jackson Laboratory, Bar Harbor, Maine. World Wide Web (www.informatics.jax.org)

Sausbier M, Hu H, Arntz C, Feil S, Kamm S, Adelsberger H, Sausbier U, Sailer CA, Feil R, Hofmann F, Korth M, Shipton MJ, Knaus HG, Wolfer DP, Pedroarena CM, Storm JF, Ruth P. Cerebellar ataxia and Purkinjie cell dysfunction caused by Ca2+-activated K+ channel deficiency. Proc Natl Acad Sci USA 2004, 101(25), 9474-8.