A Remutation to *Mbp*^{shi} named shiverer Jackson (*shi-J*)

Authors: Debra A. Thompson, Patricia F. Ward-Bailey, Leah Rae Donahue, Roderick T. Bronson and Muriel T. Davisson

Source of Support: This research was supported by grants RR001183 to the Mouse Mutant Resource (M.T. Davisson) and Cancer Center Core Grant CA34196.

Mutation (allele) symbol: *Mbp*$^{shi-J}$

Mutation (allele) name: shiverer Jackson

Gene symbol: *Mbp*

Strain of origin: BALB/cJ

Current strain name: BALB/cJ-*Mbp*$^{shi-J}$/GrsrJ

Stock #005226 (jaxmice.jax.org)

Phenotype categories: Neurological

Abstract
A neurological remutation to shiverer (a mutation in the *Mbp* gene) has been identified. This recessive mutation is recognized at 12 days of age, when the homozygotes show a generalized tremor during locomotion. The shivering phenotype becomes more severe with age and there is incoordination of the hindlimbs.

Origin and Description
Mice carrying the *Mbp*$^{shi-J}$ mutation were found by Laura Morse in Sept 2002 in a production colony of BALB/cJ mice at the Jackson Laboratory and were brought to the Mouse Mutant Research (MMR) deviant search program. Homozygous mutants are easily recognized at 12 days of age by their generalized tremor during locomotion. Weaning must be delayed *Mbp*$^{shi-J}$ homozygotes until they reach at least 5 weeks of age. This strain is maintained by cross-intercross in which obligate heterozygotes are intercrossed and homozygous offspring are bred to their +/? siblings to again generate obligate heterozygotes.

Genetic Analysis
Based on the phenotypic similarity of this new mutation to the previously described mutant shiverer (*Mbp*^{shi}), a direct test for allelism was performed by mating a male BALB/Cha.SWV(c3Fe)-*Mbp*^{shi}/J mouse to a female BALB/cJ-*Mbp*$^{shi-J}$/J. This mating produced 10 progeny of which 4 had the shiverer phenotype proving allelism.

Pathology
A routine pathological screen[1] was done with 6 mice (1 homozygous *shi-J/shi-J* mutant and 1 littermate (+/?) control pair, each at 7, 9, and 10 weeks of age). For purposes of comparison a pathological screen was also done on two homozygous shi/shi mutants and

a littermate control. The BALB/cJ-*Mbp*$^{shi\text{-}J}$/J mutants lacked CNS myelin, like the original shiverer and the controls had normal myelin.

Hearing was assessed by auditory-evoked brainstem response (ABR) testing on 2 mutants and 3 (+/?) controls. The 2.5 month-old mutants had 10 - 20 dB elevated thresholds and abnormal wave patterns with long interpeak latencies characteristic of a myelin defect. The 3 controls had normal threshold and normal interpeak latency. An electroretinogram (ERG) test was done on 2 mutants and 3 (+/?) controls and was normal.

Acknowledgements
The authors wish to thank Laura Morse for the discovery of the mutant and Heping Yu for the ABR testing, Norm Hawes for the Electroretinogram (ERG) and Coleen Marden for pathological expertise.

[1]Standard Histology Protocol used in the Mouse Mutant Resource

For fixation of tissues, mice were deeply anesthetized with tribromoethanol (avertin) until they no longer displayed a withdrawal reflex in the hind limbs and then perfused intracardially with Bouin's fixative following a flush of the vasculature with saline solution. After soaking in Bouin's for one week to demineralize bones, tissues were dissected. Six segments of spine with axial muscles and spinal cord in situ, representing cervical, thoracic and lumbar spinal segments, were dissected. The brain was removed and sliced into 6 cross sectional pieces at the levels of olfactory lobes, frontal cortex, striatum, thalamus, midbrain, rostral and caudal medulla with cerebellum. Midsagittal slices of hind leg through the knees were prepared. Slices of basal skull through the pituitary and inner ears were taken. Both eyes, salivary glands and submandibular lymph node, trachea plus thyroid and sometimes parathyroid were removed and cassetted. A longitudinal slice of skin from the back was removed. The thymus, slices of lung, and a longitudinal slice of heart were cassetted. Similarly slices of liver through gall bladder, kidney with adrenal attached, pancreas and spleen were prepared. The stomach was sliced longitudinally to include both squamous and glandular portions. Loops of small intestine from 3 levels and slices of large intestine and cecum were removed, as were slices of urinary bladder. The whole uterus, with ovaries attached, was taken. In males testes were sliced longitudinally. The accessory male organs including seminal vesicles, coagulating gland and prostate were removed en block. Altogether in most cases all tissue fit into a total of 10 cassettes. The cassettes were processed in an automatic tissue processor to dehydrate tissues which were then embedded in paraffin. Six micron sections were cut and stained with hematoxylin and eosin (H&E). Sections of brain and spinal cord in vertebral bones also were stained with luxol fast blue (LFB) for myelin and cresylecht violet (CV) for cellular detail.