Lama2$^{dy\text{-}8J}$: A new remutation to dystrophia muscularis

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Mutation (allele) symbol: *Lama2*$^{dy\text{-}8J}$

Mutation (allele) name: dystrophia muscularis 8 Jackson

Gene symbol: *Lama2*$^{dy\text{-}8J}$

Strain of origin: C57BL/6J

Current strain name: C57BL/6J-*Lama2*$^{dy\text{-}8J}$/GrsrJ

Stock #009692

Phenotype categories: neuromuscular

Abstract

We have identified a new remutation to dystrophia muscularis (*Lama2*^{dy}). Mice affected by the new *dy-8J* mutation have rear limb paralysis first noticeable at about two weeks of age, which progresses to death usually by three to four weeks of age. A direct test for allelism was set up by mating a mouse carrying the dystrophia muscularis 2 Jackson mutation to a mouse carrying this new mutation and allelism was confirmed.

Origin and Description

This remutation was first discovered by Lisa Weaver at The Jackson Laboratory in a colony of inbred C57BL/6J mice and was recognized by its smaller size and the dragging action of its hindlimbs.

Genetic Analysis

A direct test for allelism was set up by mating a B6.WK-*Lama2*$^{dy\text{-}2J}$ heterozygote to a new mutant heterozygote. This mating produced 25 progeny of which 6 were affected with the dystrophia muscularis phenotype confirming allelism. Using standard mapping techniques, affected mice from an intercross to CAST/EiJ were typed with markers on Chromosome 10, *D10Mit52* (NCBI 37 position 33.4 Mb) and *D10Mit213* (NCBI 37 position 20.1 Mb), in the region where dystrophia muscularis maps (NCBI 37 position 26.7 Mb). There was no recombination with either marker, further confirming allelism.

Pathology

The eyes of two homozygous affected animals were examined with an ophthalmoscope and the results were ambiguous. ERGs done on affected mice at three weeks of age showed abnormal rods and cones, but eyes were sent for histological examination and

were found to be normal.

Two homozygotes and two controls were tested for auditory-evoked brain stem response at twenty days of age. Homozygotes showed elevated thresholds 10-30 decibels above those of heterozygous controls, similar to results obtained in a previously published study of hearing loss in *Lama2*^{dy} mice (Pillers et al., 2002). A standard pathological screen[1] of one female and one male homozygote showed the female having myopathy with rowing of nuclei in the muscle fibers and pale staining areas in lumbar roots, and the male with severe myopathy in some muscles and some muscle with very immature fibers. This is consistent with previously reported histology of the dystrophia muscularis mutations.

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References

Pillers DA, Kempton JB, Duncan NM, Pang J, Dwinnell SJ, Trune DR. Hearing loss in the laminin-deficient *dy* mouse model of congenital muscular dystrophy. Mol Genet Metab. 2002 Jul;76(3): 217-24.

Protocols

[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.