Severe Runting (*sevr*): A New Mouse Mutation on Chromosome 18

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Mutation (allele) symbol: *sevr*

Mutation (allele) name: severe runting

Gene symbol: *sevr*

Strain of origin: C3H/HeJ

Current strain name: C3H/HeJ-*sevr*/GrsrJ

Stock #006247 (jaxmice.jax.org)

Phenotype categories: size, skeletal

Abstract
A new autosomal recessive mutation has been identified and named severe runting (*sevr*). This mutation when homozygous causes a reduced body size, slight tremors, and a shortened lifespan with many animals dying by weaning. This mutation maps to Chromosome 18.

Origin and Description
This new mutation arose in a colony of inbred C3H/HeJ mice in the Mouse Mutant Resource at The Jackson Laboratory in 1998 and was discovered by Karen Smith. The *sevr* mutants were first observed because of their unusually small size. Homozygotes are characterized at about two weeks of age as having a smaller body size than their littermates and by a high mortality rate at approximately four weeks of age. Slight tremors in homozygotes are often observed before death. The *sevr* colony is maintained by progeny tests and heterozygous pairs produce close to the expected 25% homozygotes.

A *sevr*/*sevr* mutant in the lower right corner compared to the larger littermate control on the left.

Genetic Analysis

Using the standard mapping procedures of The Mouse Mutant Resource, an intercross was set up by mating two female CAST/Ei mice to a male heterozygous for the severe runting mutation. No affected mutant mice were observed in the 51 progeny produced by this cross. The tested heterozygous F1 progeny from this cross were then intercrossed and in four matings produced 47 affected progeny out of 485 total born for 9.7% expression (less than the expected 25%). Using standard PCR techniques and DNA from 33 F2 progeny from the previous cross for linkage analysis, the severe runting mutation was mapped to Chromosome 18 proximal to *D18Mit40.*

Pathology

A standard pathological screen[1] of 9 mutant mice between 5 weeks and 4 months of age showed atrophy of the thymus, which is typical of wasting mice, and no other consistent lesions.

Hearing was assessed by auditory brain stem response testing of one homozygote and one heterozygote at 35 days of age and two mutants and two controls at 25 days of age. All mutant and control mice had normal ABR thresholds indicating good hearing.

The eyes of two mutant and two control animals at 3 weeks of age were examined with an ophthalmoscope and they were determined to be normal for their age.

Histology was done on the eyes of one homozygous mutant and they were normal except that they have retinal degeneration 1 (*rd1*), which is a characteristic of the C3H background strain and not caused by this new mutation.

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[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.