Dominant tail short: A New Dominant Skeletal Mutation maps to Chromosome 1

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Mutation (allele) symbol: *Dts*

Mutation (allele) name: Dominant tail short

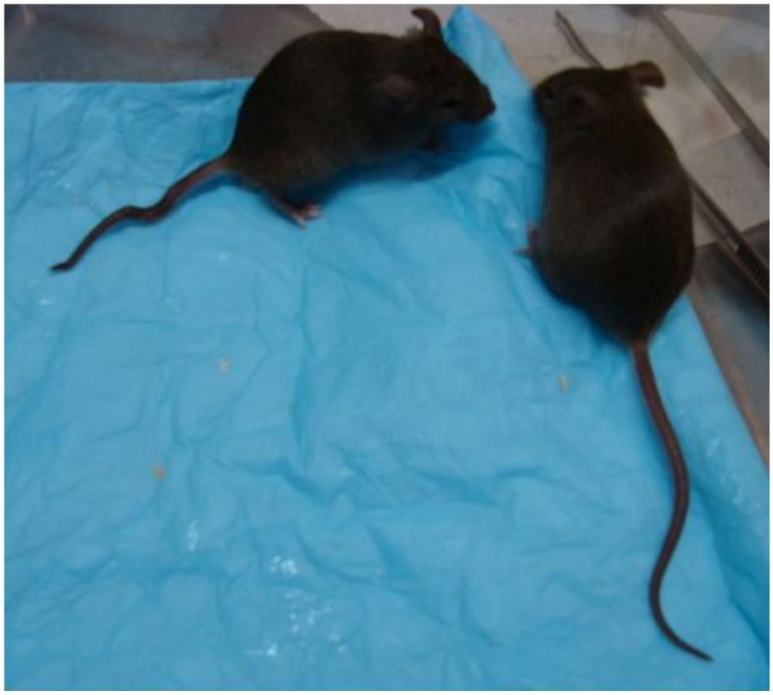
Gene symbol: *Dts*

Strain of origin: CBA/J

Stock #013084 (jaxmice.jax.org)

Phenotype categories: skeletal, development

Abstract
We have identified a new dominant mouse mutation recognized by its shortened, kinked tail. There is variable expressivity in the length of the tail and the number of tail kinks. A backcross to C57BL/6J was used to map the new mutation to Chromosome 1.



Dts/+ at 8 weeks of age on the left and wild type sibling on the right

Origin and Description
Mice displaying the new *Dts* mutation were discovered by Amy Leighton at The Jackson Laboratory in the year 2000 in a production colony of CBA/J. These mice were sent to the Mouse Mutant Resource for analysis and affected F1 offspring from an outcross to

C57BL/6J proved the mutation dominant. Heterozygotes display a shortened, kinked tail (see photo). The number of kinks in the tail varies from carrier to carrier and an assessment by palpation of 8 mutants showed an average number of tail kinks to be approximately 3.6. The maximum number of tail kinks found so far is 5. The length of the tail varies from one quarter normal length to three quarters normal length. Mild hydrocephalus and aberrant cells in the testis have also been associated with this mutation, although fertility seems normal. The CBA/J background strain is prone to seizures, and seizures have been observed in some of the *Dts* mutant mice as the mice age. Consistent with Mendelian prediction for a fully penetrant dominant, approximately 50% of the offspring from heterozygote x wild type matings are mutants. However, progeny testing of a small population of mutant offspring from heterozygous intercrosses showed that all mutant offspring were heterozygotes and no homozygotes were identified.

Genetic Analysis

Using the standard mapping protocols of The Mouse Mutant Resource the new *Dts* mutation was mapped to Chromosome 1. Linkage was first seen using the MIT marker *D1Mit181* (NCBI 37 position 74.5 Mb) that showed 9.5% recombination. Further mapping has determined that the mutation is located within the first 64.46 Mb of Chromosome 1. A proximal marker to narrow the critical region has not yet been identified, but the data are completely concordant from 6.46 Mb-43.51 Mb, with the first discordant samples at 64.46 Mb.

Pathology

A routine pathological screen[1] was performed on one ten-month-old, two four-month-old and two three-month-old mutants. The ten-month-old male showed a few large aberrant cells in the testis and mild hydrocephalus. One four-month-old lactating female had mild hydrocephalus and acute tracheitis. One four-month-old male had mild hydrocephalus and large aberrant cells in the testis. The cerebral aqueducts of one three-month-old female were dilated. The same female and a three-month-old male were found to have retinal degeneration consistent with homozygosity for the $Pde6b^{rd1}$ mutation, which is a strain characteristic of CBA/J.

Hearing, as assessed by auditory brainstem response testing (ABR), performed on two four month old male *Dts* heterozygotes and controls showed normal hearing.

The eyes of two *Dts* mutant mice were screened with an ophthalmoscope and one affected male had a white cornea in the right eye and one small eye. All displayed retinal degeneration consistent with the $Pde6b^{rd1}$ of the CBA/J background.

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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.