A kinked tail mutation on Mouse Chromosome 5 named jagged tail-like

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Mutation (allele) symbol: *jgl*

Mutation (allele) name: jagged tail-like

Gene symbol: *jgl*

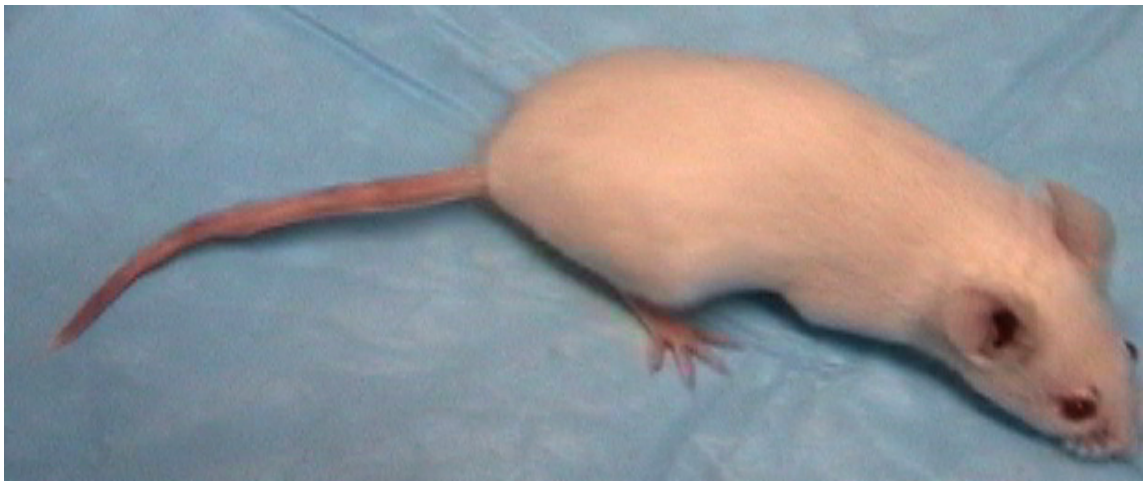
Strain of origin: BALB/cByJ-*Clcn1*$^{adr\text{-}mto2J}$/J

Current strain name: BALB/cByJ-*Clcn1*$^{adr\text{-}mto2J}$-*jgl*/GrsrJ

Stock #003922 (jaxmice.jax.org)

Phenotype categories: extremities: tail; reproductive system: abnormalities

Abstract
An autosomal recessive tail mutation named jagged tail-like has been found in the Mouse Mutant Resource (MMR) at The Jackson Laboratory. Homozygotes are easily characterized by their kinked tails that are recognizable by 10 days of age. In both male and female mutants reproductive tract abnormalities are seen. Most homozygous mutants are not fertile, however a few have produced litters. Spleens of affected animals were atrophic. This mutation maps to Chromosome 5 and may be a remutation to jagged tail *jg*.



Origin and Description

This spontaneous mutation was found in the BALB/cByJ-*Clcn1*$^{adr\text{-}mto2J}$/J strain in the Mouse Mutant Resource in1998. Mutant mice are recognized by their kinked tails. In both male and female mutants their reproductive organs are smaller than normal and males have testicular abnormalities. Spleens of affected animals were atrophic especially

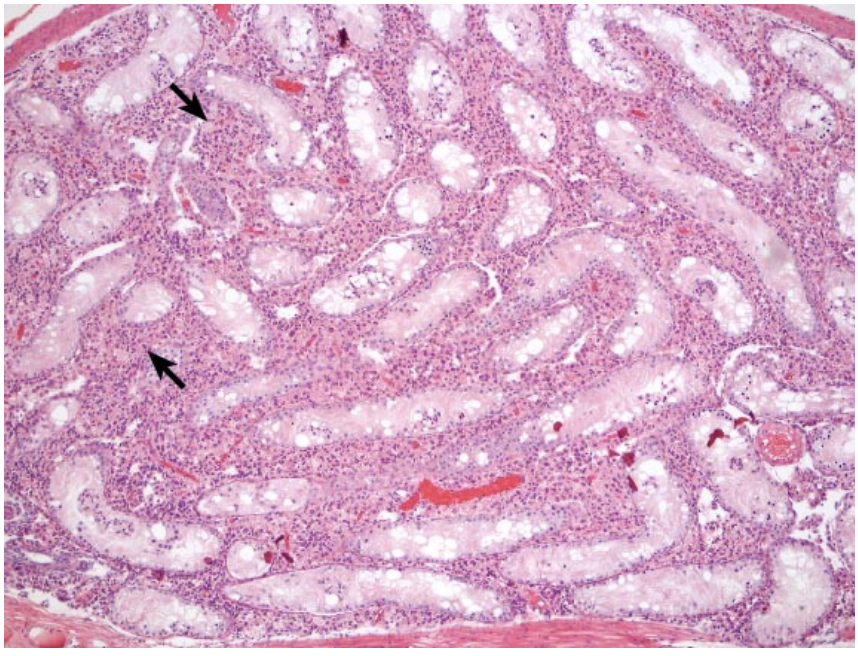
in the white pulp. Because most homozygous mutants are not fertile, the strain is maintained by test matings.

Genetic Analysis

Using the standard mapping protocols of The Mouse Mutant Resource, two +/*jgl* mice were crossed to two CAST/Ei mice and produced no affected progeny. F1 progeny were intercrossed and tested matings produced 27 F2 affected animals of which 21 were used to determine the chromosomal location of the jagged tail-like mutation. A genome wide scan was done using a pooled DNA sample made from the DNA of the affected animals in the linkage cross. Linkage on Chromosome 5 was first detected with *D5Mit9* and *D5Mit51*. The individual DNA samples from the linkage cross were then typed for these two markers and seven additional Chr 5 markers. The recombination estimates with standard errors and the best gene order are: centromere-- [*D5mit229, D5Mit22, D5Mit9*]--2.5 +/-2.5-- [*D5Mit239, D5Mit24, D5Mit25*] -- 9.6 +/- 5.0 --*jgl*--2.5+/- 2.5 --*D5Mit291* --7.6 +/- 4.5-- *D5Mit 325*--7.3+/- 4.3-- *D5Mit51*. Gene order and recombination frequencies were calculated with the Map Manger computer program (Manley 1993). The complete Chr 5 linkage data for 21 F2 *jgl/jgl* mice has been deposited in the Mouse Genome Database, accession #J:85852. Based on the Ensembl assembly for Chr 5, the chromosomal position for *jgl* is between 111050412 bp (*D5Mit25* at 61 cM) and 123577767 bp (*D5Mit291* at 70 cM). This may be a remutation to jagged tail (*jg*), a mouse mutation that maps at 67 cM on Chr 5, but a test for allelism was not done because *jg* is cryopreserved only.

Pathology

A routine histological screen[1] of two 5-month-old homozygous mutants showed abnormal vertebral bodies that were large and misshapen. Long bones and thoracic and lumbar vertebrae appear normal. Longitudinal sections of the spine were normal. Sections of the reproductive tract of thirteen homozygous males had severe atrophy of the seminiferous tubules and hyperplasia of the Leydig cells.



Histological section showing atrophy of the seminiferous tubules and hyperplasia of the Leydig cells (arrows).

Female reproductive tracts appear normal, though may be smaller. The spleens of two 6 week-old affected animals were atrophic, especially in the white pulp. All other organs appear normal.

X-rays of two mutant mice demonstrate the tail phenotype.

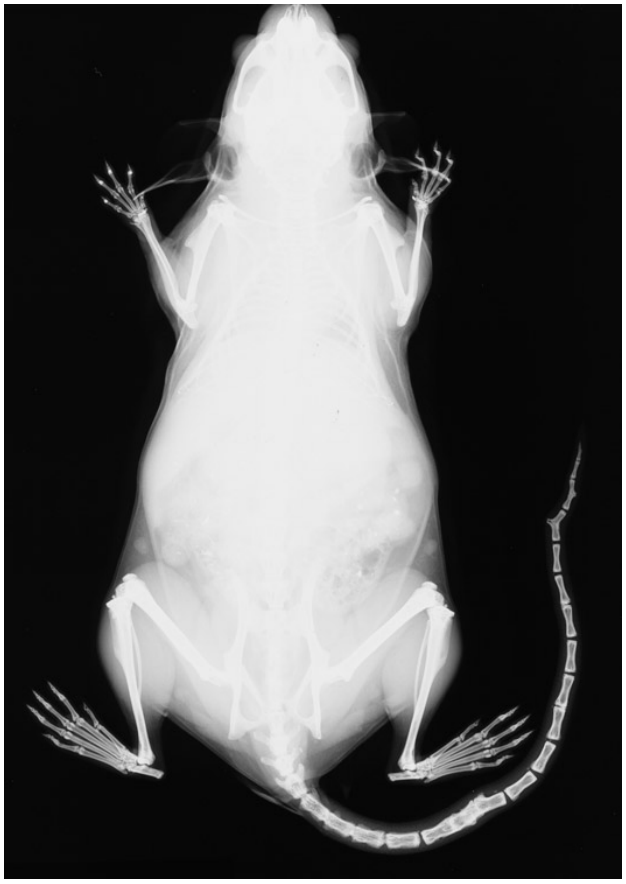


Figure 1

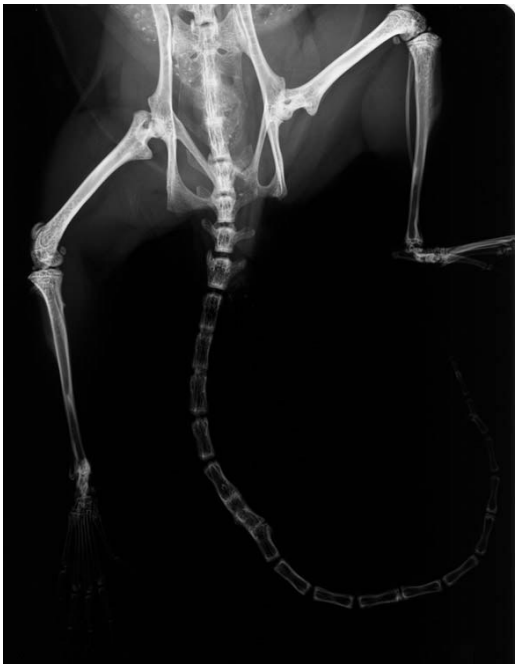


Figure 2

Figure 1: a whole body x-ray (3x, Faxitron X-ray, Wheeling, IL) of a homozygous female *jgl/jgl* mouse at 4 months of age. The most obvious skeletal abnormalities are fusions of tail vertebrae (5,6, & 7) and exostoses of vertebrae near the tail tip. Unlike the original jagged tail mutant, *jgl/jgl* mice do not have shorter tails than littermates although the kinking may make them appear that way. Exostoses also can be seen in the phalanges of all four feet.

Figure 2: a 5x x-ray of the lower extremities of the same mouse. Although the long bones appear to be slightly under mineralized, there are no morphological abnormalities.

Auditory brainstem response (ABR) testing (Zheng et al.) was done on four homozygotes and four controls at 4-5 weeks of age. Hearing was determined to be normal in all mice tested.

The eyes of four mutant and four control animals at 4-5 weeks of age were examined with an ophthalmoscope and all were normal. The eyes of two mutants and three controls were also examined at 9 weeks of age ands all were normal.

Acknowledgements
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References

Manley KF (1993) A MacIntosh program for storage and analysis of experimental mapping data. Mamm Genome 4, 303-313.

Mouse Genome Database (MGD) Mouse Genome Informatics Project, The Jackson Laboratory, Bar, Harbor, Maine. October 2003 (www.informatics.jax.org)

Zheng QY, Johnson KR, Erway LC(1999) Assessment of hearing in 80 inbred strains of mice by ABR threshold analyses. Hear Res 130, 94-107.

[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.