# Trembler-like: A new dominant neurological mutation on Chromosome 11

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Mutation (allele) symbol: *Trl*

Mutation (allele) name: Trembler-like

Gene symbol: *Trl*

Strain of origin: C57BL/6J-Tg(RP24-226L7)28Dn

Current strain name: C3FeLe.B6-*a Trl*/J

Stock #008425 (jaxmice.jax.org)

Phenotype categories: Neurological

**Abstract**
A new dominant mutation that causes affected mice to tremble has been identified and has been mapped to Chromosome 11 in the same region as trembler ($Pmp22^{Tr}$). Because *Tr* is a dominant allele, a direct test for allelism was inconclusive between trembler and mice carrying this new mutation.

**Origin and Description**
Mice carrying this new spontaneous mutation were discovered in a research colony of C57BL/6J-Tg(RP24-226L7)28Dn mice at the Jackson Laboratory. Mutant mice are recognized at about 3 weeks of age by tremors and an abnormal gait. C3FeLe.B6-*a Trl*/J heterozygous male mice have a high rate of being non-productive, therefore the colony is maintained by mating a heterozygous female (+/*Trl*) and a (+/+) male C3FeLe.B6-*a*/J (Stock #000198). Backcrossing every generation has eliminated the RP24-226L7 transgene from the background strain.

**Genetic Analysis**
Using the standard mapping protocols of The Mouse Mutant Resource, C3FeLe.B6-*a Trl*/J mice were mated to CAST/Ei. The affected progeny from these matings were then backcrossed to a C3FeLe.B6-*a*/J and the progeny were used for linkage analysis. This mutation was mapped proximal to *D11Mit349* (55.6 Mb) and distal to *D11Mit90* (70.3 Mb).

**Pathology**
A pathological screen[1] of three heterozygous mice was performed at 35, 41 and 64 weeks of age. Myelin was absent from peripheral nerves, which appeared enlarged. Peripheral hypomyelination is characteristic of previously described *Pmp2* mutations.

The eyes of a heterozygous mutant at 11 months of age were examined with an ophthalmoscope and electroretinogram tests (ERG) were performed. The results were all normal.

Hearing as assessed by auditory brainstem response testing of three heterozygous mutants at 4 weeks of age revealed that two mice had normal hearing and the third mouse had a slightly elevated threshold.

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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.