Reeler 5 Jackson, a remutation of the *Reln* gene

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Mutation (allele) symbol: *Reln*$^{rl\text{-}5J}$

Mutation (allele) name: reeler 5 Jackson

Gene symbol: *Reln*

Strain of origin: C3Fe.SWV-*Mbp*^{shi}/J

Current strain name: C3Fe(SWV)-*Mbp*^{shi} *Reln*$^{rl\text{-}5J}$/GrsrJ

Stock #005562 (jaxmice.jax.org)

Phenotype categories: neurological

Abstract
We have identified a new remutation of the reelin (Reln) gene by a direct test for allelism. The phenotype, described below, is the same as the original reeler (*rl*) mutation.

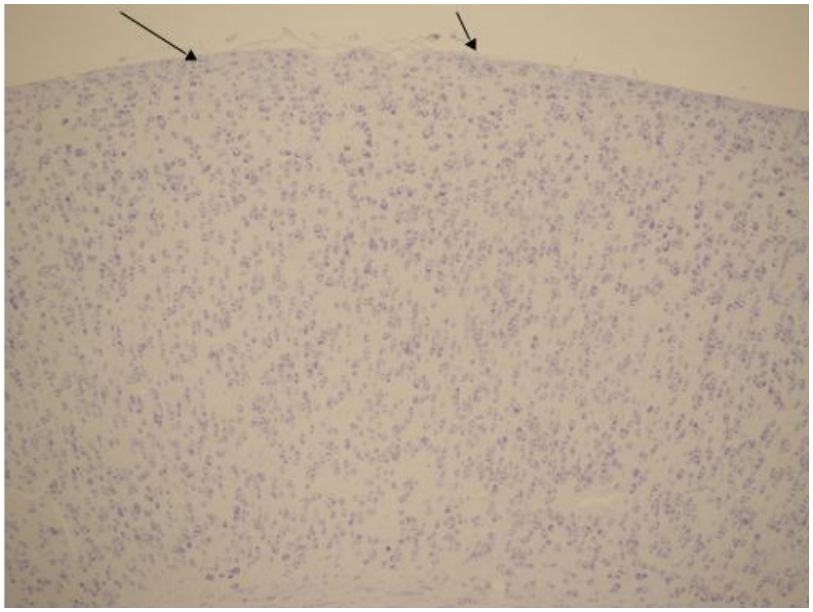
Origin and Description
The *Reln*$^{rl\text{-}5J}$ remutation was discovered at The Jackson Laboratory in 2004 by Amanda Bragg in a production colony of C3Fe.SWV-*Mbp*^{shi}/J mice (Stock #001428). Mice homozygous for this spontaneous, recessive remutation of reeler can be recognized by two weeks of age. They have difficulty with locomotion that causes a leaning side-to-side behavior as they walk. Like original reeler homozygotes, *rl-5J* mutants are unable to keep their hindquaters upright and frequently fall over on their sides. Females homozygous for this new remutation do breed, but male homozygotes have not. Both sexes live to adulthood. Heterozygotes for this remutation are normal.

Genetic Analysis
In order to determine the mode of inheritance, a female homozygote was mated to an unrelated C56BL/6J male. No affected offspring were observed in the F1 generation produced from this mating. Mice from this F1 generation were then mated together to produce F2s, and in this cross both affected and unaffected animals were produced, proving that the mutation is recessive.

A direct test for allelism was performed by mating two heterozygous B6C3Fe *a/a-Relnrl*/J females to a heterozygous new mutant male. This mating produced two litters in which three offspring out of fifteen born were affected with the reeler phenotype, proving the new mutation to be an allele of the *Reln* gene.

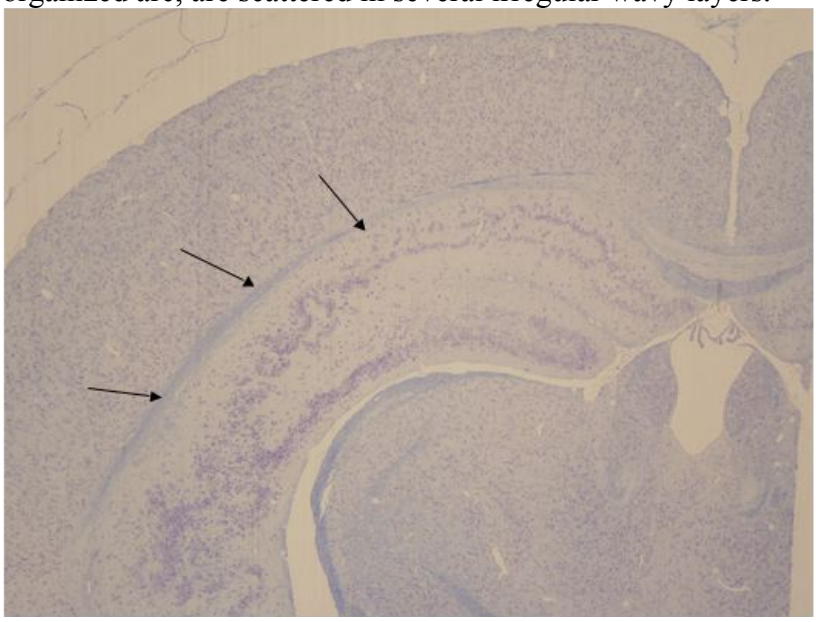
Pathology

A routine pathological screen[1] done on three mice homozygous for *rl-5J* and one control littermate showed that the neuropathology in the mutants is identical to that described for the original reeler mutation (MGD 2005); the control was normal. In mice homozygous for *rl-5J,* the cortex has scrambled layering. Most noticeably, the outer marginal layer, which is normally relatively cell-free, has many cells.



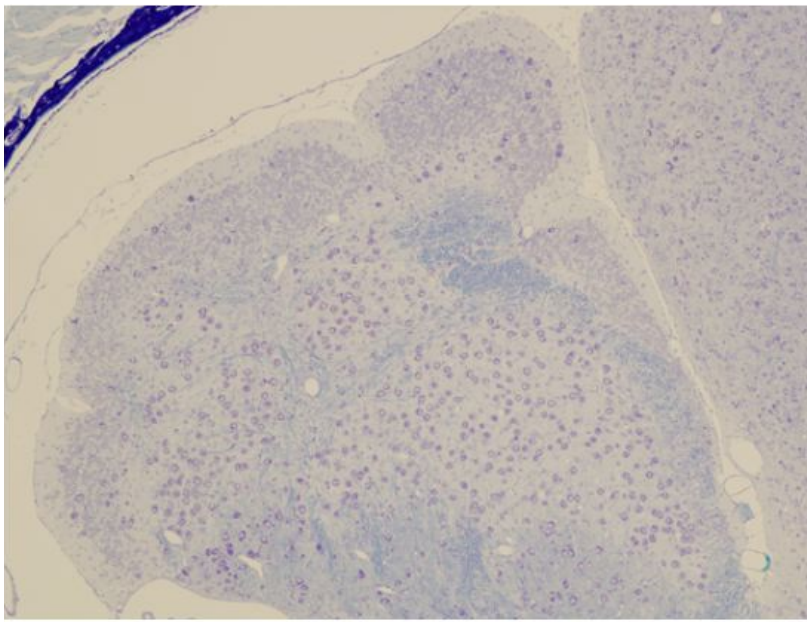
The cortex of a mouse homozygous for the *rl-5J* mutation showing scrambled layering.

In the hippocampus the neurons of the hippocamal gyrus, instead of being aligned in an organized arc, are scattered in several irregular wavy layers.



The hippocampus from a mouse homozygous for *rl-5J* showing neurons scattered in several irregular layers. (20X)

The cerebellum is small with scrambled Purkinjie and granule cells.



The cerebellum from a mouse homozygous for the *rl-5J* mutation showing scrambled Purkinje and granule cells

Hearing tests as assessed by auditory brain stem response (ABR) on individual animals showed normal thresholds and wave pattern. Eye examination showed all animals had retinal degeneration-1; which is a characteristic of the C3Fe.SWV-*Mbp*^{shi}/J strain and not caused by the *rl-5J* mutation.

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

[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.