Reeler 4 Jackson (*Reln*$^{rl\text{-}4J}$), a remutation of the *Reln* gene

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Gene symbol: *Reln*

Mutation (allele) symbol: *rl-4J*

Mutation (allele) name: reeler 4 Jackson

Strain of origin: B6.129-*Irf1*^{tm1Mak}

Current strain name: B6.Cg-*Reln*$^{rl\text{-}4J}$/GrsrJ

Stock #005250 (jaxmice.jax.org)

Phenotype categories: size, neurological

Abstract
We have identified the fourth allele of the reelin (*Reln*) gene by a direct test for allelism. Both the phenotype and pathology described below, are the same as the original reeler (*rl*) mutation with the exception that this new remutation has earlier lethality.

Origin and Description
The *Reln*$^{rl\text{-}4J}$ remutation was discovered at the Jackson Laboratory in 2003 by Tina Morse in a production colony of B6.129-*Irf1*^{tm1Mak} mice. Mice homozygous for the *Reln*$^{rl\text{-}4J}$ remutation can be recognized by two weeks of age. They have difficulty with locomotion that causes a leaning side-to-side behavior as they walk and are smaller than their unaffected littermates. Like the original reeler homozygotes, *rl-4J* mutants are unable to keep there hindquaters upright and frequently fall over on their sides. Some mice homzygous for the *Reln*$^{rl\text{-}4J}$ remutation die by weaning age but others housed with their parents have lived longer. Both male and female heterozygotes breed and live a normal life span.

Genetic Analysis
In order to determine the mode of inheritance, a female homozygote was mated to an unrelated C57BL/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 a female homozygote B6C3Fe-*a*/*a*-*Reln*^{rl}/J mouse to a male heterozygous for this new remutation. This mating produced 21 offspring in 6 litters, of which 7 progeny were

affected with the *Reln*^{rl} phenotype, proving the new mutation to be an allele of the *Reln* gene.

Pathology

A routine pathological screen of two mice homozygous for the *Reln*$^{rl\text{-}4J}$ mutation at 3 weeks and 3.5 weeks of age and a control at 3.5 weeks of age showed that the neuropathology of the brain is identical to that described for the original reeler mutation (MGD 2008); the control was normal. The mutants displayed the "scrambled" cerebellum and cortex seen in the original reeler mutation and all other reeler alleles. The *Reln*$^{rl\text{-}4J}$ mutants showed scrambled layering in the cortex, neurons of the hippocampal gyrus are scattered in irregular wavy layer and the cerebellum is smaller with scrambled Purkinjie and granule cells.

Discussion

The *Reln*$^{rl\text{-}4J}$ mutation, like the *Reln*$^{rl\text{-}7J}$ mutation, causes earlier lethality than the original *Reln*^{rl} which may be due to a strain background effect. The original *Reln*^{rl} is maintained on a hybrid background (rl/rl X B6C3F1).

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