Waved 3 Jackson; a new remutation in the *Ppp1r13l* gene.

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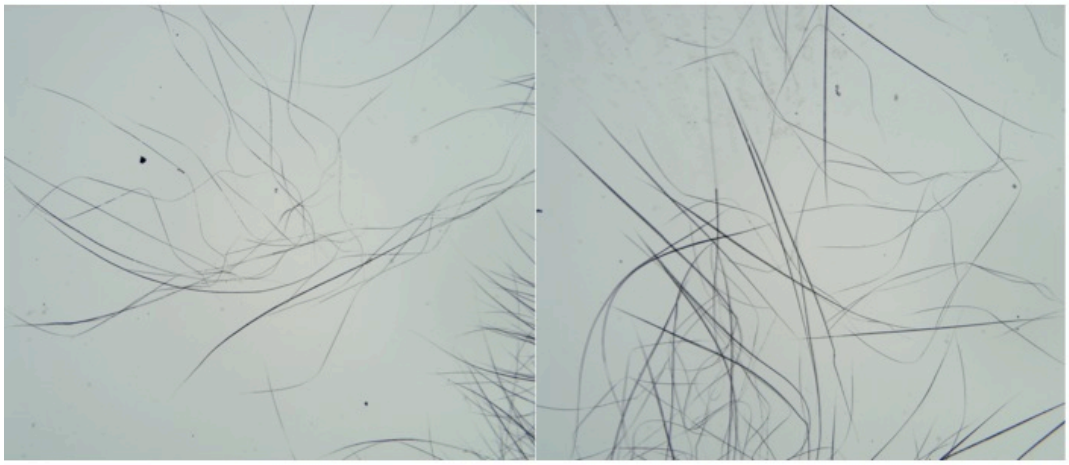
Source of Support: This research was supported by NIH/NCRR grant RR01183 to the Mouse Mutant Resource (M.T. Davisson, PI) and Cancer Center Core Grant CA34196

Mutation (allele) symbol: *Ppp1r13l*$^{wa3\text{-}J}$
Mutation (allele) name: waved 3 Jackson
Gene symbol: *Ppp1r13l*
Strain of origin: BALB/cJ
Current strain name: BALB/cJ-*Ppp1r13l*$^{wa3\text{-}J}$/J
Stock #007971 (jaxmice.jax.org)
Phenotype categories: Hair and eye abnormalities and congestive heart failure.

Abstract
A new spontaneous recessive remutation has been identified and characterized as a cardiomyopathy, including abnormal hair and damaged eyes. Identical phenotypes, map location, and a sequence analysis comparison determined this new mutation to be a remutation of *Ppp1r13l*^{wa3}.

Origin and Description
The new spontaneous, recessive waved 3 Jackson remutation arose in a production colony of BALB/cJ mice at the Jackson Laboratory. This mutation displays an abnormal hair coat, damaged eyes and cardiomyopathy. The eyes of waved 3-Jackson mice are open at birth, which results in eye injuries and loss of sight. The coats of waved 3 Jackson mutants are sparse**.** The waved 3 Jackson mutant mice develop an early-onset cardiomyopathy, which leads to congestive heart failure and eventually death. The lifespan is shorter than normal but variable. Most mutants die by 6 months of age, but some have lived longer. Homozygous waved 3 Jackson females are not able to breed. Homozygous mutant males may breed once or twice in their lifetime but often fail to breed. This colony is also maintained by ovarian transplantation.

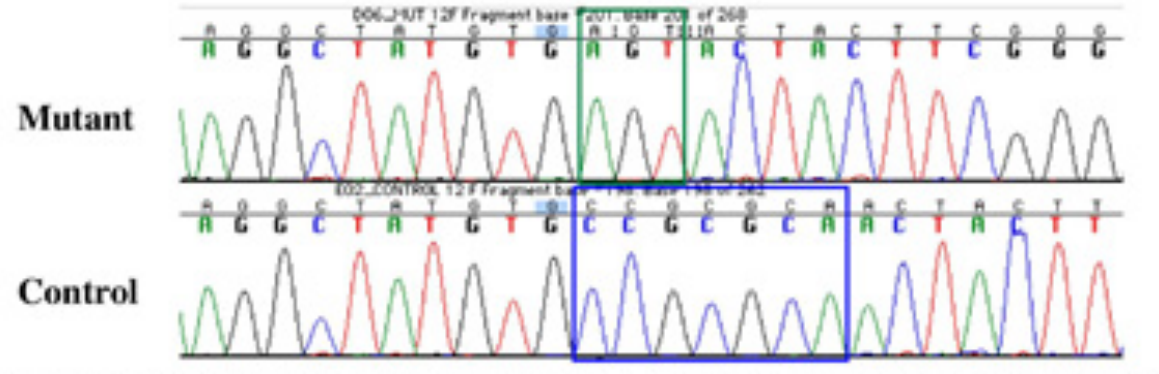


Hair pluck taken from a homozygous *Ppp1r13l*^{wa3} mutant is shown on the left and hair from a littermate control is shown on the right. Note the thin hair from the mutant mouse.

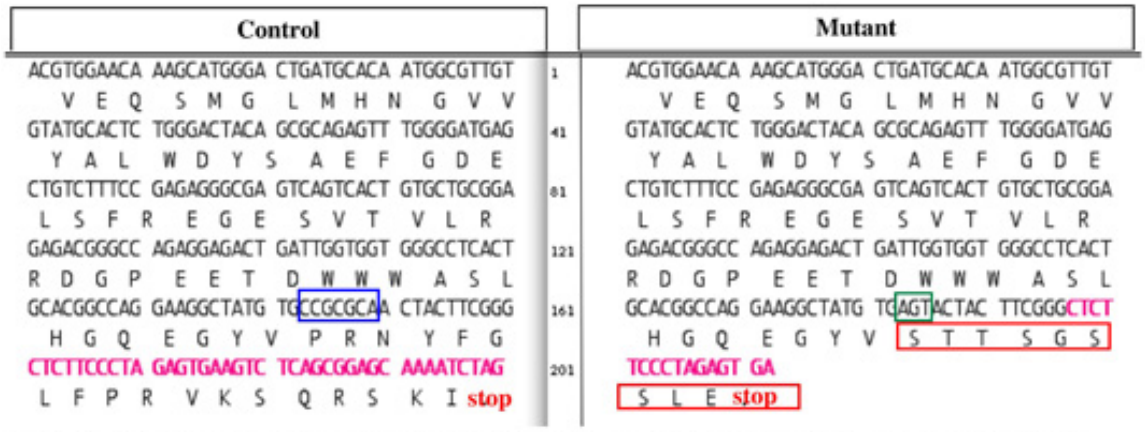
Genetic Analysis

A homozygous waved 3 Jackson mouse was mated with a C57BL/6J mouse. The F1 hybrid mice produced from this cross had a normal looking phenotype, proving that this mutation has recessive inheritance. The F1 hybrid mice were then intercrossed and produced 92 F2 affected mice that were used for linkage analysis.

Using our standard mapping procedures, this new remutation was mapped to Chromosome 7 between *D7Mit306* (NCBI 36 position 10.9mb) and *D7Mit341* (NCBI 36 position 25.1mb). Based on phenotype and map location, *Ppp1r13l* was thought to be a good candidate gene for this new mutation. Sequence analysis revealed a mutation in exon 12. The PCR product from genomic DNA used to sequence the mutation was generated by primers that produce a 330 base pair product specific to the coding region of *Ppp1r13l*; primer exon 12 Left (CCATCCTTCCTGTGGCTG) and primer exon 12 Right (ATAACAGATCAGCTTGGCCC).



Comparison of DNA sequence chromatograms of the homozygous *wa3-J* mutant (top) and +/+ control (bottom). The green and blue boxed regions correspond to the green and blue boxed regions shown in the amino acid sequence below.



Exon 12 of *Ppp1r13l* (black) and coding region of exon 13 (magenta). The control DNA sequence and its amino acid translation are shown on the left, and the *wa3-J* mutant DNA and its translation on the right. The seven nucleotides deleted in the mutant sequence are enclosed by a blue box in the control sequence, and the three nucleotides inserted in the mutant sequence are enclosed by a green box in the mutant sequence. The mutation is predicted to cause nine amino acid substitutions followed by a premature stop codon (enclosed by red box).

Pathology
The phenotype of *wa3-J* appears to be the same as that described for the original waved 3 mutation. A routine pathological examination of one homozygous waved 3-Jackson mouse at 10 weeks of age revealed an enlarged heart. The atria were also abnormally large. One homozygous waved 3 Jackson mouse at 3 weeks of age had a thin skin. The eyes of one mutant mouse at age 7 weeks were tested by an electroretinogram (ERG) and were found to have no cones. Mutant pups with open eyelids at birth also had a white vascular cornea, which can affect the ERG results. Hearing as assessed by auditory brainstem response testing (ABR) of one waved 3-Jackson mutant mouse at 8 weeks of age showed normal hearing.

Acknowledgements
The authors thank Linda Washburn for discovery of the mutant, Roderick Bronson and Coleen Kane for pathological screening, Chantal Longo-guess for hearing assessment, and Norm Hawes and Ron Hurd for eye examinations.

References
J: 96392 Herron BJ et al., "A mutation in NFkB interacting protein 1 results in cardiomyopathy and abnormal skin development in wa3 mice." Hum Mol Genet 2005 Mar 1; 14(5): 667-77