Long john 4 Jackson (*lgj-4J*); A new remutation in the *Npr3* gene

Belinda Harris, Patricia Ward-Bailey, Kenneth Johnson, and Roderick Bronson

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Mutation (allele) symbol: $Npr3^{lgj-4J}$

Mutation (allele) name: longjohn 4 Jackson

Gene symbol: $Npr3^{lgj-4J}$

Strain of origin: NOD/ShiLtJ-*wly*/J

Current strain name: NOD/*shi*LtJ-$Npr3^{lgj-4J}$/J

Stock #008254 (Available only as DNA from The Jackson Laboratory DNA Resource)

Phenotype categories: skeletal/limbs

Abstract
We have identified a new remutation in the *Npr3* gene which exhibits the same phenotype as the original long john mutation ($Npr3^{lgj}$) on Chromosome 15.

Origin and Description
This new spontaneous remutation was found in a research colony of NOD/ShiLtJ-*wly*/J (wooly) mice in The Jackson Laboratory Mouse Mutant Resource in 2003. Like the previously described longjohn (*lgj*) mutation, homozygous $Npr3^{lgj-4J}$/J mutant mice are easily distinguishable as early as 5-7 days of age by their elongated bodies, kinked tails and conical extension of the body. $Npr3^{lgj-4J}$/J mutant mice have extra long bones, especially the digit and have kyphosis. Mice carrying the $Npr3^{lgj-4J}$/J mutation are viable and fertile.

Genetic Analysis
Using the standard mapping procedures of the Mouse Mutant Resource, a mouse homozygous for the $Npr3^{lgj-4J}$ mutation was mated to a C57BL/6J mouse. The F1 progeny from this cross were then intercrossed and produced 54 affected mice of which 21 were utilized for linkage analysis. The $Npr3^{lgj-4J}$ mutation maps to Chromosome 15 proximal to *D15Mit175* (NCBI 36 position 9.2 Mb) and distal to *D15Mit229* (NCBI 36 position 41.9 Mb) and is non-recombinant with *D15Mit265* (NCBI 36 position 12.9Mb) . Based on phenotype and map position similarities, a direct test for allelism was set up by mating a female mouse homozygous for the $Npr3^{lgj-4J}$ mutation to a male mouse carrying the $Npr3^{lgj}$ mutation. This mating produced two affected mice out of 16 born with two born dead proving allelism.

Pathology
Our standard pathological screen showed that one nine week old homozygous $Npr3^{lgj-4J}$

male had a very odd shaped head where the cerebellum is, cervical area tissue appeared to have an open spine, and the mouse had otitis media. X-Rays done on one three week old homozygous male showed elongated long bones and spine. Hearing as assessed by auditory brainstem response testing (ABR) on one homozygote male and two control females showed all tested to be almost deaf by three months of age. This hearing loss due to age related hearing loss in the background NOD/shiLtJ-wly/J strain. The eyes of two male homozygotes and two female and three male controls were examined with an ophthalmoscope and were determined to be normal.

Discussion

We have identified a remutation to longjohn with similarities to the original mutation on Chromosome 15. This remutation will be available from The Jackson Laboratory DNA Resource and no embryos will be cryopreserved.

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