Loop tail-like; a semi-dominant skeletal mutation on Chromosome 1.

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Mutation (allele) name: loop tail-like

Gene symbol: *Lootl*

Strain of origin: B6.129S7-Gt(ROSA)26Sor/J (Stock #002192)

Current strain name: B6.Cg-*Lootl*/GrsrJ

Stock #013121 (jaxmice.jax.org)

Phenotype categories: skeletal

Abstract
We have identified a semi-dominant mouse mutation with very low penetrance on the C57BL/6J background, that we named loop tail-like. This new mutation causes affected heterozygous and homozygous mice to have a short curled tails and some affected heterozygotes mice may also display Spina bifida at birth. No homozygotes with Spina bifida have been observed. Wild type siblings are phenotypically normal. The loop tail-like mutation is mapped to Chromosome 1, near the location of the gene *Vangl2* (NCBI 37 position 173.9.0Mb).

Origin and Description
Mice carrying the loop tail-like mutation were discovered by Jason Fuller in an Induced Mutant Resource colony of B6.129S7-Gt(ROSA)26Sor/J mice at The Jackson Laboratory and were recognized by their short curled tails. Some affected mice have been observed to produce newborns with spina bifida in varying degrees of severity, which usually die shortly after birth. Occasionally one with mild spina bifida may live and produce offspring, but progeny tests have identified them as heterozygotes. This colony is maintained by mating C57BL/6J female mice with homozygous *lootl* male mice and then intercrossing their obligate heterozygous offspring. In heterozygous matings less than the expected ratio of 25% is observed, which could be the result of in utero lethality. Both heterozygotes and wild types live a normal lifespan. Most female homozygotes have a closed vagina and do not breed.

Genetic Analysis
Using the standard mapping protocols of The Mouse Mutant Resource an intercross was set up by mating an unrelated C3H/HeSnJ female mouse to a male mouse affected by the *Lootl* mutation. No mutant mice were observed in the F1 progeny produced by this cross. The F1 mice were then mated together and *Lootl* mice were observed in the F2 progeny. Twenty-one of the F2 mice were used for linkage analysis. Linkage was found on Chromosome 1 and the *Lootl* mutation was positioned between *D1Mit33* (NCBI 37 position 160.3Mb) and *D1Mit403* (NCBI 37 position 177.5 Mb) and is non-recombinant with *D1Mit15* (NCBI 37 position 170.2 Mb) and *D1Mit150* (NCBI 37 position 176.5Mb).

The *Vangl2* gene (NCBI 37 position 173.9.0Mb) was thought to be a plausible candidate gene and some sequencing was done, but not all exons could be tested. Therefore, based on phenotype and map position this mutation was named loop tail-like.

Pathology

No lesions were found in a routine pathological screen on a five-month-old male mutant. Hearing as assessed by auditory brainstem response (ABR) testing of two female and two male heterozygotes was normal.

The eyes of seven mutant mice were examined with and ophthalmoscope. One female heterozygote showed an iris coloboma with a normal retina and one wild type female had a retinal white area. Eyes of three male heterozygotes and two female wild types were normal.

Discussion

We report a new mutation named Loop tail-like which maps to Chromosome 1 in the same location as the original loop tail mutation (*Vangl2*^{Lp}). Similar to the original *Vangl2*^{Lp} mutation, all heterozygotes have normal hearing. Unlike the *Vangl2*^{Lp} mutants, the head movement of loop tail-like mice appears normal.

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