Curvy tail: a new skeletal mutation that maps to Chromosome 16

Belinda S. Harris, Patricia F. Ward-Bailey, David E. Bergstrom, Roderick T. Bronson and Leah Rae Donahue.

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

Mutation (allele) symbol: *Clec16a*^{curt}

Mutation (allele) name: curvy tail

Gene symbol: *Clec16a*

Strain of origin: SWR/J-*Clcn1*$^{adr\text{-}mto}$/J

Current strain name: SWR/J-*Clec16a*^{curt}/GrsrJ

Stock #014631

Phenotype categories: skeletal, neurological

Abstract
We have identified a new skeletal mouse mutation that causes a curvy tail, small body size, squinting eyes, and digits that are crooked and curve toward the outside of the body. Curvy tail homozygotes may live to adulthood but die prematurely and do not breed. Heterozygotes live a normal lifespan and are fertile. Curvy tail was mapped using an intercross with CAST/EiJ and was found to be on Chromosome 16.

Origin and Description
Curvy tail (*curt*) mice were discovered by Leigh Ann Kulla in a colony of SWR/J-*Clcn1*$^{adr\text{-}mto}$/J mice in the Mouse Mutant Resource at The Jackson Laboratory in 2002. The myotonia mutation was bred out of this mutant subline. *curt* mutants were first recognized phenotypically by an odd S-shaped tail. They are approximately 50% the weight of their unaffected littermates at one month of age, they have small, partially closed, squinting eyes throughout their lifetimes, and their digits are crooked and curve outward away from the body. Homozygotes may live until adulthood, but most die by 3 months of age and, to date, none has reproduced. This new mutation is maintained by intercrossing progeny tested heterozygotes, which live a normal lifespan and have normal fertility. Intercrossing heterozygotes produces less than the expected number of homozygotes. Fifty-three homozygotes were identified out of 328 born with 9 of those 328 missing at wean age and 13 born dead. This is a yield of only 16.16% homozygotes indicating some prewean loss of homozygotes. If the missing and born dead animals that were recorded are assumed to have been homozygotes and added to the 53 phenotypic homozygotes, the yield is closer to the expected 25% homozygotes (75/328=22.9%).

Genetic Analysis
Using our standard mapping protocols an intercross to CAST/EiJ positioned the *curt* mutation on Chromosome 16. The *curt* mutation maps between *D16Mit122* (NCBI 37

position 7.44 Mb) and *D16Mit88* (NCBI 37 position 13.2 Mb) and is non-recombinant with *D16Mit87* (NCBI 37 position 9.81 Mb).

Pathology

Hearing as assessed by auditory brainstem response testing of two seven-week-old homozygous females showed severe hearing loss while four heterozygotes all had normal hearing. The eyes of 2 heterozygotes and 2 homozygotes were examined with an ophthalmoscope and, independent of the retinal degeneration associated with *Pde6b*^{rd1} from this genetic background, the eyes were all normal. A routine pathological screen showed synovial hyperplasia in one knee and ectopic Purkinje cells in the molecular layer of an eight-week-old male homozygote. X-rays showed no bone abnormalities in one female and one male homozygote at five weeks of age, yet the female had thickened periosteum and thickened synovium of the knee. The digits did not show any disproportionate lengths.

Acknowledgements

The authors thank Bo Chang for eye examinations, Chantal Longo Guess for ABR testing, and Coleen Kane for histological preparations.

Addendum

In late 2012 this mutation was found to be a small deletion in *Clec16a*.