A new, spontaneous short nose mutation in the mouse collagen type 2 alpha 1 gene

Authors: Michelle M. Curtain, Louise Dionne, Heather E. Fairfield, and Leah Rae Donahue, Ph.D.

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Mutation (allele) symbol: *Col2a1*^{M3J}

Mutation (allele) name: mutation 3 Jackson

Gene symbol: *Col2a1*

Strain of origin: C57BL/6J-*Kit*$^{W\text{-}v}$/J

Current Strain Name: B6(Cg)-*Col2a1*^{M3J}/GrsrJ

Stock #016585 (jaxmice.jax.org)

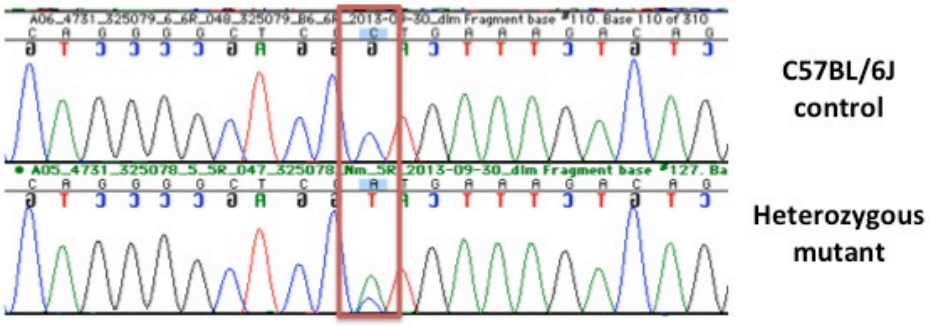
Phenotype category: craniofacial

Origin and Description:

In July, 2010, a mutation causing a shortened nose was identified at The Jackson Laboratory in the strain C57BL/6J-*Kit*$^{W\text{-}v}$/J (stock #000049). The *Kit*$^{W\text{-}v}$ mutation was backcrossed out of this mutant subline and the shortened face phenotype persisted unaltered.

Left: short nose mutant. *At right*: a normal sibling

Genetic Analysis:
A shortened nose mutant was outcrossed to a C57BL/6J mouse and two out of three F1 offspring exhibited the shortened nose phenotype, proving this mutation dominant. The colony has been maintained by breeding a heterozygous animal to a wildtype sibling. To find the genetic map position, a mutant was outcrossed to a BALB/cByJ and affected F1 hybrids were backcrossed to C57BL/6J. DNA was prepared from affected and unaffected mice from this N2 population and sent to The Jackson Laboratory Fine Mapping Laboratory, where this mutation was mapped to Chromosome 15. Whole exome sequencing from heterozygotes revealed a single nucleotide transversion of C to A on Chromosome 15, at position 97,817,272 (GRCm38). Subsequent Sanger sequence analysis of genomic DNA confirmed the presence of this single point mutation from C to A on Chromosome 15 (see chromatogram). This sequence change is predicted to affect normal splicing in collagen type 2 alpha 1 (*Col2a1*), as the mutation resides within the splice acceptor site adjacent to exon 26. Being the third mutation in this gene identified at The Jackson Laboratory, this mutation has been designated *Col2a1*^{M3J}.



Comparison of sequence chromatograms from C57BL/6J control and heterozygous mutant samples. The red box indicates a heterozygous single nucleotide variant in mutant samples at Chr15: 97,817,272 (MGSCv37) or Chr15: 97,986,841 (GRCm38), confirming the exome sequencing result.

Pathology:
Routine pathological screening was conducted, and did not show any aberrations. An ophthalmoscope was used to view the eyes of three mutants (two female and one male) and three controls (two female and one male) at two months of age, and one mutant and two controls at four months of age; all were normal Hearing was assessed by auditory brainstem response threshold analysis. Two heterozygotes assessed at two months of age were found to have normal hearing, and two separate heterozygotes assessed at four months of age were found to have slightly elevated thresholds at 16 and 32kHz.

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