Underwhite 7 Jackson, a spontaneous point mutation in *Slc45a2*

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Mutation (allele) symbol: *Slc45a2*$^{uw\text{-}7J}$

Mutation (allele) name: underwhite 7 Jackson

Gene symbol: *Slc45a2*

Strain of origin: C3H/HeJ-*Mfs*/J

Current strain name: C3H/HeJ-*Slc45a2*$^{uw\text{-}7J}$/GrsrJ

Stock #019114 (jaxmice.jax.org)

Phenotype categories: Coat color

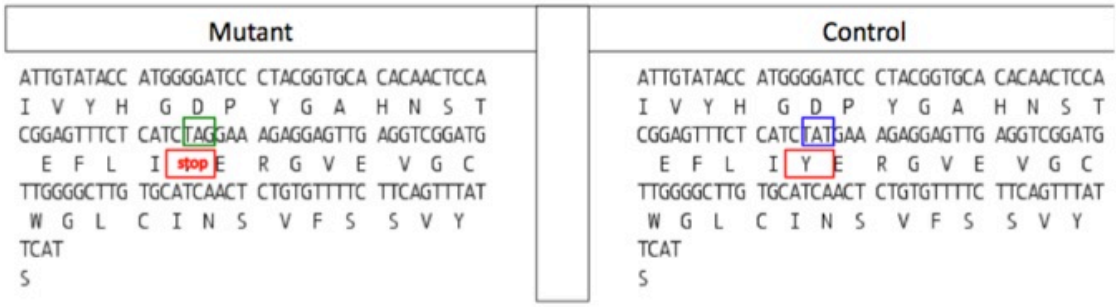
Abstract
A new recessive mutation that causes diluted coat color has been characterized and identified as a point mutation of the solute carrier family 45, member 2 (*Slc45a2*) by its map position on Chromosome 15, coat color phenotype, and Sanger sequencing based determination of the mutation.

Origin and Description
A new spontaneous, recessive mutation was discovered by Belinda Harris in a colony of C3H/HeJ-*Mfs*/J at The Jackson Laboratory in 2011. Mice homozygous for this new mutation can first be identified by light colored skin in newborn pups in comparison to their littermates. The coats of mice homozygous for this mutation have a dirty white color on this agouti background. Mutants have red eyes at an early age, and when the mutants get older their eyes become darker. Homozygous mice are fertile and live a normal life span. The dominant *Mfs* mutation was easily bred out of this mutant subline by one outcross to C3H/HeJ, and the resulting strain has been subsequently maintained by sibling inbreeding heterozygous females with homozygous males.

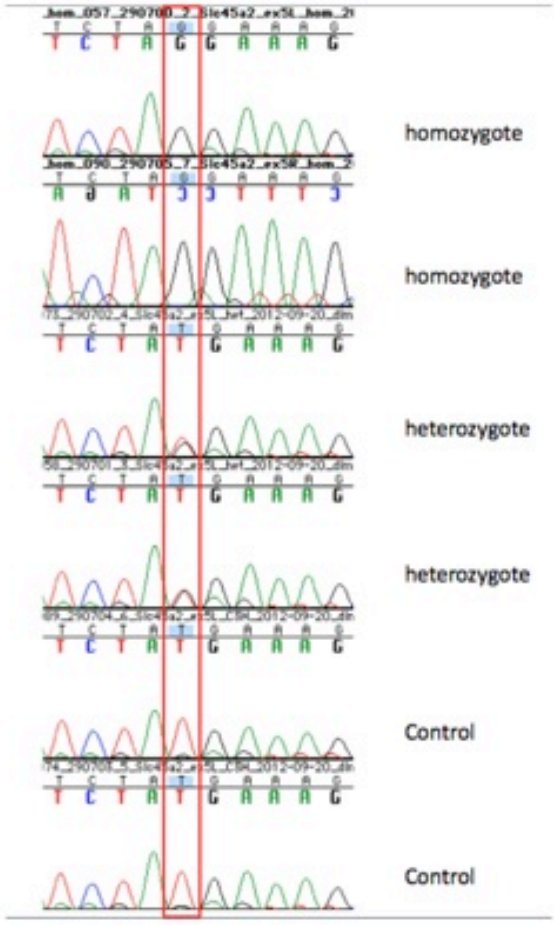
Genetic Analysis
Mutant animals in the C3H/HeJ-*Mfs*/J mutant subline were outcrossed to 129S1/SvImJ mice to establish heritability. No affected mice were found in the F1 generation. Intercrossing of unaffected F1 animals resulted in affected F2 animals, indicating a recessive mode of inheritance. Affected F2 mice were generated for linkage analysis and fine mapping. Using standard SNP protocols, linkage analysis for this mutation was completed in the Fine Mapping Laboratory at The Jackson Laboratory. This mutation mapped to Chromosome 15, between NCBI 37 position 03094890 bp and NCBI 37 position 22857571 bp.

Based on coat color phenotype and location within the mapped critical interval, solute carrier family 45, member 2 (*Slc45a2*) was considered a plausible candidate gene. Primers were generated that produce a 504 base pair product spanning the predicted

mutation: Slc45a2 Exon5 Left (TGGTAGAAAAAGGACCCGTAAA) and Slc45a2 Exon5 Right (CACTTCCTGTGATCCTCTTGAA). Sequence analysis of two mutant genomic DNA samples compared to genomic DNA from four unaffected animals confirmed a single nucleotide transition from T to G at position 10953155 in *Slc45a2*. This is a nonsense mutation that is predicted to cause one amino acid deletion followed by a premature stop codon at protein position 292. This mutant provides a model for type IV oculocutaneous albinism.



A portion of the protein coding region of *Slc45a2*. The control DNA sequence and its amino acid translation are shown on the right, and the *Slc45a2*$^{uw\text{-}7J}$ mutant DNA and its translation on the left. A single nucleotide transition is enclosed by a green box in the mutant sequence and a blue box in the control sequence. The mutation is predicted to cause a one amino acid deletion followed by a premature stop codon (in the red box).



Comparison of DNA sequence chromatograms from *Slc45a2*$^{uw\text{-}7J}$ homozygote, heterozygote and control. The red boxed region corresponds to the green and blue boxed regions in the sequence figure.

Pathology
Hearing, assessed by auditory brainstem response testing (ABR) of one mutant and one control mouse, showed normal hearing at 11 weeks of age. The eyes of one mutant and one heterozygote at 14 weeks of age were tested by electroretinography and both mutant and heterozygote were found to have a retinal degeneration phenotype consistent with the *pde6b*^{rd1} mutation, which is a strain characteristic of C3H/HeJ and thus not attributable to the underwhite 7 Jackson mutation.

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