Underwhite 6 Jackson, a new spontaneous mutation in *Slc45a2*

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Mutation (allele) symbol: *Slc45a2*$^{uw\text{-}6J}$

Mutation (allele) name: underwhite 6 Jackson

Gene symbol: *Slc45a2*

Strain of origin: CAST/EiJ

Current strain name: CAST/EiJ-*Slc45a2*$^{uw\text{-}6J}$/GrsrJ

Stock #008544 (jaxmice.jax.org)

Phenotype categories: Coat color

Origin and Description
A new spontaneous recessive mutation was discovered by Jennie Davis in a colony of CAST/EiJ at The Jackson Laboratory in 2007. Mice homozygous for this new mutation can first be identified by light colored skin in newborn pups when compared to their littermates. The coats of mice homozygous for this mutation have a dirty white color. 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.

Genetic Analysis
Mutant animals were outcrossed to C57BL/6J 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. This mutation mapped to Chromosome 15, between NCBI 37 position 03410212 bp and NCBI 37 position 25965349 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. A direct allele test was set up by mating a mouse heterozygous for this new mutant with a mouse homozygous for *Slc45a2*$^{uw\text{-}7J}$. This mating produced 6 progeny of which 3 expressed the mutant phenotype, proving this new mutation to be an allele of *Slc45a2*. This mutant provides a model for type IV oculocutaneous albinism. Because The CAST/EiJ genetic background will not successfully cryo-recover, sperm was cryopreserved from heterozygous males that had been generated from C57BL/6J females bred to CAST/EiJ-*Slc45a2*$^{uw\text{-}6J}$/GrsrJ homozygous males.

Pathology

A routine pathological screen of one mutant at the age of 5 weeks showed no lesions. Hearing, assessed by auditory brainstem response testing[1] (ABR) of one mutant and two controls at 4 weeks age and one mutant and two controls at 30 weeks age showed no elevated thresholds, while ABR of two mutants at 17 weeks age showed slightly elevated thresholds in one, but normal readings in the other. The eyes of two mutants and at 17 weeks of age were tested by electroretinography and found to have normal readings.

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[1] ABR thresholds in mice are determined using a semi-automated computer system (Intelligent Hearing Systems, Miami, Florida). Subdermal needle electrodes are inserted at the vertex and ventrolaterally to both ears of anesthetized mice. Specific auditory stimuli from 10-100 dB SPL are delivered binaurally through plastic tubes from high frequency transducers. ABR thresholds are obtained, in an acoustic chamber, for clicks and for 8, 16, and 32 kHz pure-tone pips.