Steel 24 Jackson: a recessive mutation in the Kit ligand gene

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Mutation (allele) symbol: *Kitl*$^{sl\text{-}24J}$

Mutation (allele) name: Steel 24 Jackson

Strain of origin: B6;129S1-*Il1rap*^{tm1Roml}/J

Current strain name: B6;129S1- *a Kitl*$^{sl\text{-}24J}$/GrsrJ

Stock #014608 (jaxmice.jax.org)

Phenoytpe Categories: pigmentation

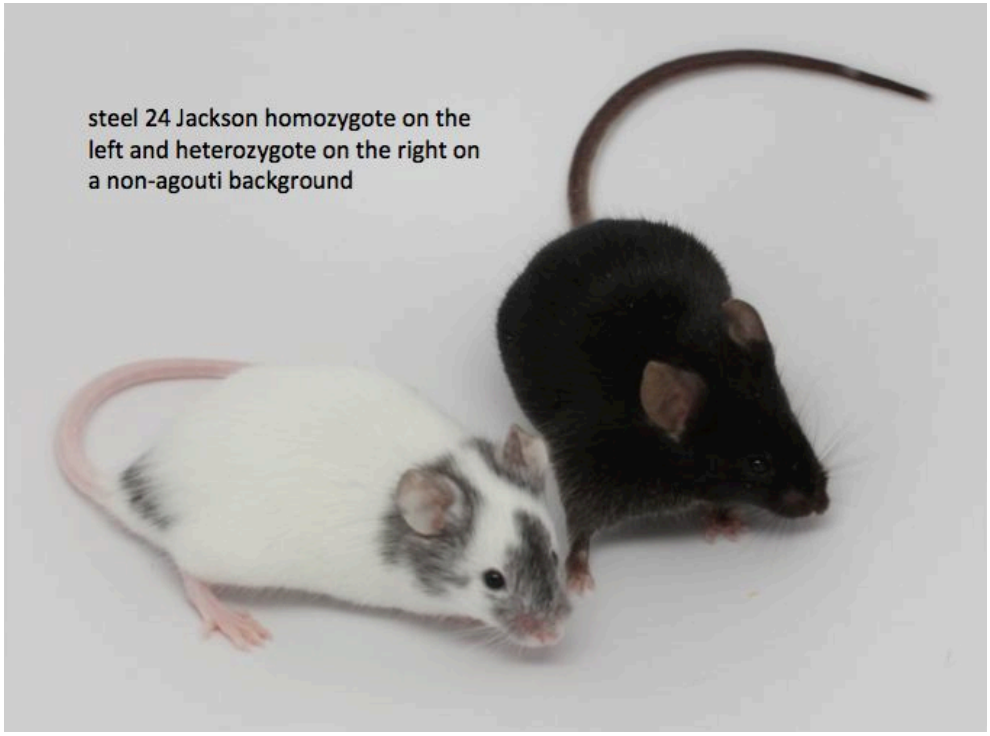
Origin and description
A spotted coat mutation was discovered at The Jackson Laboratory in B6;129S1-*Il1rap*^{tm1Roml}/J, (Stock #003284), a strain then segregating for agouti and non-agouti. Mutants are white with pigmented spotting on the head and rump. They have white feet, tail, and vibrissae and have a slightly smaller body size when young, but no size difference is evident in adults. In the presence of the dominant agouti allele homozygous mutants are white with agouti colored spots while on a non-agouti black background homozygotes are white with black spots (see photo on allele detail page). Homozygotes are viable and fertile. Homozygotes of either gender are mated to littermate controls for colony maintenance. Through selective breeding the agouti allele has been bred out of this mutant subline, which is now homozygous for nonagouti. No reduced fertility was found for either gender of homozygote.

Genetic Analysis
To determine inheritance, a mutant with black spots from the B6;129S1 segregating background was outcrossed to a mouse of the C57BL/6J strain (Stock#000664) to generate F1 hybrid offspring. The F1 hybrids were all non-agouti black. These obligate heterozygotes were intercrossed to generate F2's and the spotted mutation was observed, proving its recessive inheritance pattern.

We mapped this mutation using our standard mapping protocol. Homozygotes were outcrossed to CAST/EiJ and the F1 hybrid offspring were then intercrossed to generate F2 mutants. DNA from F2 mutant and unaffected mice were submitted to The Jackson Laboratory Fine Mapping Laboratory and this mutation was found to map to Chromosome 10 between markers *D10Mit291* at 95.7 Mb and *D10Mit70* at 103.5 Mb. This map location includes the Kit ligand gene (at 99.4 Mb), a gene in which previously identified mutations have caused spotted pigmentation. Thus, an allele test was done by breeding a homozygous mutant of this newest strain with compound heterozygotes from

the strain WCB6F1/J-*Kitl*^{Sl}/*Kitl*$^{Sl\text{-}d}$. All of the offspring of this cross had the mutant phenotype, confirming that this new mutation is an allele of *Kitl*. This new, recessive mutation has been designated as the steel 24 Jackson allele of Kit ligand (*Kitl*$^{sl\text{-}24J}$).

It should be noted that all of the offspring from the allele test had a phenotype that was identical to the *sl-24J* and did not match either of the alleles present in WCB6F1/J-*Kitl*^{Sl}/*Kitl*$^{Sl\text{-}d}$. The *Kitl* alleles show a range of pigmentation with *Kitl*^{Sl}/+ on this genetic background showing grey with infrequent belly spots, *Kitl*$^{Sl\text{-}d}$/+ on this genetic background showing dark grey with a white head blaze, and when these two alleles are combined in a compound heterozygote the mice are white with black eyes.



Pathology
Routine pathological screening was performed on two mutant mice and two control mice. All results were normal. An ophthalmoscope was used to view the eyes of two mutant mice and two control mice and no abnormalities were detected. Hearing was assessed by auditory-evoked brainstem response threshold analysis and no abnormalities in hearing were detected.

Discussion
Most steel mutations are either dominant or semi-dominant and female infertility is often found in viable homozygotes. This new spontaneous steel mutation has an outward phenotype that is recessive and no impairment of fertility has been detected. Due to its interesting phenotype and unusual mode of inheritance, further studies may be undertaken to further characterize the mutant phenotype and identify the causative mutation.

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