A new mouse mutation named semidominant lethal spotting is mapped to Chromosome 2

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Mutation (allele) symbol: *Sls*

Mutation (allele) name: Semidominant lethal spotting

Gene symbol: *Sls* (may be an allele of Edn3)

Strain of origin: C57BL/6J

Current strain name: C57BL/6J-*Sls*/GrsrJ

Stock #005135 (jaxmice.jax.org)

Phenotype categories: skin and hair, homozygous lethal at weaning

Abstract
A new mutation named semidominant lethal spotting (*Sls*) arose on the C57BL/6J strain in the Mouse Mutant Resource at the Jackson Laboratory. Mice homozygous for this semidominant mutation may exhibit megacolon ending in lethality. Coat color varies from a large area of white spotting in the homozygote at weaning age, small white spots on the belly in the heterozygotes, and normal black coat color in the wild type. This mutation has been mapped to the same chromosomal region of Chromosome 2 as $Edn3^{ls}$ (lethal spotting).

Origin and Description
The *Sls* mutation arose on C57BL/6J and is maintained by heterozygote x wild type matings. When heterozygotes are mated together, 3 distinct phenotypes are produced. At weaning age, a large area of white spotting in the homozygote is seen, small white spots on the belly in the heterozygotes, and normal black coat color in the wild type. When two wild type animals are mated together they produce only wild type animals.

Genetic Analysis
Using our standard mapping protocols a C57BL/6J-*Sls*/+ mouse was mated to a CAST/Ei mouse to produce F1s. The F1 progeny were then intercrossed and produced the F2 progeny used to map this mutation. The F1 progeny produced by this mapping cross to CAST/Ei were all normal appearing, but when mated together produced 3 distinct phenotypes. The *Sls* mutation maps between *D2Mit113* and *D2Mit148* and is non-recombinant with *D2Mit213*. Genetic linkage and marker order were analyzed with the Map Manager software program (Manley, 1993). The recombination estimates with standard errors and best gene order are: centromere-[*D2Mit51*] -17.3 +/- 7.2 - [*D2Mit113*] - 2.4 +/- 2.4 - [*D2Mit213*, ***Sls***] - 2.4 +/- 2.4 - [*D2Mit148*] - 4.8 +/- 3.4 - [*D2Mit200*].

Based on the Ensembl assembly Build 32 for Chromosome 2, our non-recombinant marker *D2Mit213* is at 175.1 mb and *Edn3*^{ls} (lethal spotting) is at 175.3mb.

Pathology

Our standard pathological screen showed hydronephrosis and hydrocephalus in one mutant, but other heterozygotes showed no lesions. Some homozygotes had megacolon. Hearing assessed by ABR testing and ophthalmoscopic eye tests showed both mutants and controls are normal.

Discussion

This mutation was named semidominant lethal spotting to indicate similarity with but differences from the original lethal spotting. In comparison with lethal spotting, *Sls* is semidominant, has a severe, sometimes lethal phenotype in the homozygote, a mild spotting phenotype in the heterozygote, a normal black coat in the wild type. *Sls* is probably allelic with the lethal spotting mutation (*Edn3*^{ls}) because of its chromosomal position and similar phenotype. A direct test for allelism was not possible because *Edn3*^{ls} is now available only as cryopreserved embryos.

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References

Manley KF (1993) A MacIntosh program for storage and analysis of experimental mapping data. Mamm Genome 4,303-313

Mouse Genome Database (MGD) Mouse Genome Informatics Project, The Jackson Laboratory, Bar Harbor, Maine.