Variable spot and size: A new dominant spotting mutation on mouse Chromosome 2

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Mutation (allele) symbol: *Vss*

Mutation (allele) name: variable spot and size

Gene symbol: *Vss*

Strain of origin: B6EiC3Sn-*a*/*A*-*Gy*/J

Current strain name: B6EiC3-*a*/*A*-*Vss*/GrsrJ

Stock #006450 (jaxmice.jax.org)

Phenotype categories: color, size

Abstract
A new dominant spotting mutation named Variable Spot and Size (*Vss*) has been found at The Jackson Laboratory. In comparison to their normal littermates, mice heterozygous for the *Vss* mutation are recognized by a small, variably sized belly spot and an overall smaller body size. A linkage cross to CAST/Ei was utilized to map this mutation to Chromosome 2.

A Vss/+ mouse showing the white belly spot is seen on the left and a littermate control is shown on the right. Both are 3.5 weeks of age.

Origin and Description
This mutation was discovered by Jane Farley in a colony of B6EiC3Sn-*a*/*A*-Gy/J mice at The Jackson Laboratory. Mice carrying the *Vss* mutation are recognized as having a white belly spot and an overall smaller body size. Both male and female heterozygotes are viable, live a normal lifespan, and breed well. This colony is maintained by mating heterozygous *Vss* mice to the B6EiC3H-*a*/*A* F1 background strain.

A small sized mouse carrying the *Vss* mutation (*Vss*/+) is shown on the left and a larger (+/+) littermate control is shown on the right. Bother are 2.5 weeks of age.

Genetic Analysis

Using our standard mapping protocols, a CAST/Ei mouse was mated to a heterozygote *Vss* mouse and produced 13 mutants out of 32 progeny in the F1 generation. Some progeny produced from this mating displayed the *Vss* phenotype proving dominant inheritance. The CAST/*Vss* F1s were backcrossed to wildtype B6EiC3H-a/A F1 mice and produced 285 progeny that were used to map *Vss* to Chromosome 2. The *Vss* mutation was mapped between *D2Mit124*, which had 8 recombinants out of 61 meioses, and *D2Mit17*, which had 3 recombinants out of 40 meioses.

Pathology

Eight heterozygous *Vss* mice and littermate controls were sent to pathology for a routine pathological screen. Four of the *Vss* mice 2-3.5 months of age were found to have no gross abnormalities. Four *Vss* mice aged 16-18 months showed lesions such as degeneration of the liver and abnormal cells in the pancreas, which are common in older animals and probably not the result of the *Vss* mutation.

Auditory brainstem response testing was done on four heterozygotes and five controls; all mice tested were found to have normal hearing.

Eyes of two *Vss* heterozygote mutants and controls at four and seven months of age were examined with an ophthalmoscope and found to be normal.

Discussion

We report a new spotting mutation named variable spot and size (*Vss*), which appears as a small to large sized white belly spot on the affected mice, as well as having a smaller body size than littermates. It has been mapped to Chromosome 2. A search in Mouse Genome Informatics (MGI) for other mutations causing color spotting and small body size yielded *Pax6* (NCBIm36 position 105.4 Mb), which may be a candidate gene for *Vss*.

The *Pax6* mutants however also show a wide range of eye, craniofacial, and forebrain phenotypes that are not observed in the *Vss* mutant mice. A previously described mutant, lethal spotting ($Edn3^{ls}$) with a similar phenotype also maps to Chromosome 2, but is more distal at (NCBIm36 position 174.4 Mb) and was ruled out as a candidate gene.

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