Extra-toes spotting-like: a polydactyly and color spotting mutation on Chromosome 7

Richard M. Samples, Patricia F. Ward-Bailey, Jieping Wang, Leah Rae Donahue, Roderick T. Bronson, and Muriel T. Davisson

Source of Support: The research was supported by NIH/NCRR grant RR01183 to the Mouse Mutant Resources (M.T.Davisson,PI) and Cancer Center Core Grant CA34196.

Mutation (allele) symbol: *Xsl*

Mutation (allele) name: extra-toes spotting-like

Gene symbol: *Eif3c*

Strain of origin: C3HeB/FeJ

Current strain name: C3HeB/FeJ-*Eif3c*^{Xsl}/GrsrJ

Stock #006045 (jaxmice.jax.org)

Phenotype categories: skeletal and color spotting

Abstract
A spontaneous, dominant mutation causing extra-toes and a coat color spotting phenotype has been named extra-toes spotting-like (*Xsl*) .The similarity of phenotype and Chromosome 7 map position suggest that this new mutation may be a remutation to extra-toes spotting (*Xs*), however a direct test for allelism was not performed because *Xs* is only available as frozen embryos.

Origin and Description
The extra-toes spotting-like (*Xsl*) mutation was discovered by Brent Foster in a production colony of C3HeB/FeJ mice (stock #000658) in AX-9 at The Jackson Laboratory on August 9, 2000. Mice heterozygous for *Xsl* have a belly spot and extra toes at the thumb position on one or both front paws. These heterozygous mice are smaller than wildtype littermates up to weaning age (3 weeks), but catch up to normal size by 6 weeks.

Genetic Analysis
In order to determine the mode of inheritance a mouse carrying the *Xsl* mutation was crossed to an inbred C3HeB/FeJ mouse. This mating generated 13 mice in two litters of which 4 were affected proving dominant inheritance. Using our standard mapping procedures a backcross was set up by mating a C3HeB/FeJ-*Xsl*/J female mouse to a CAST/Ei mouse and then backcrossing the progeny to a C3HeB/FeJ +/+ female or male mouse. This mating generated 66 affected animals that were used for linkage analysis. The *Xsl* mutation maps on mouse Chromosome 7 between *D7Mit9* (NCBIm34 position-117.5) and *D7Mit43* (NCBIm34 position 124.4 Mb) and is non-recombinant with *D7Mit105* (NCBIm34 position 122.6 Mb).

Pathology
A routine pathological screen of a mutant and control at 4 weeks of age showed no lesions. The hearing as assessed by ABR of 2 mutants and 1 control at 4 weeks of age was normal. The eyes of all genotypes (2 mutants and 1 control at 4 weeks of age) were examined with an ophthalmoscope and all are affected with retinal degeneration 1 (*pde6b*^{rd1}*)* which is a characteristic of the C3HeB/FeJ background strain and not the result of the *Xsl* mutation.

Acknowledgements
The authors wish to thank Brent Foster for the discovery of the mutant, Heping Yu for hearing tests, Norm Hawes for eye examinations, and Coleen Marden for her excellent technical assistance.

Addendum
The extra-toes spotting like mutation was found to be an intragenic deletion in the eukaryotic translation initiation factor 3 subunit C gene, predicted to result in a 19 amino acid deletion. Therefore, this mutation is allelic with extra-toes spotting. See Gildea et al., FASEB J 2011, 25(5) p1596.