Two mutations in the *Lmbr1* and *Hx* region of mouse Chromosome 5

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Mutation (allele) symbols: *Hxl* and *Hxl2*

Mutation (allele) names: hemimelic extra toes-like and hemimelic extra toes-like 2

Strain names: B10.PL-$H2^{u}$-*H2-T18*^{a}/(73NS)/Sn-*Hxl/Grsr*J and B6;129P3-*Hxl2/Grsr*J

Stock #003561 for *Hxl* (jaxmice.jax.org)
Stock #004689 for *Hxl2,* available as DNA from The Jackson Laboratory DNA Resource

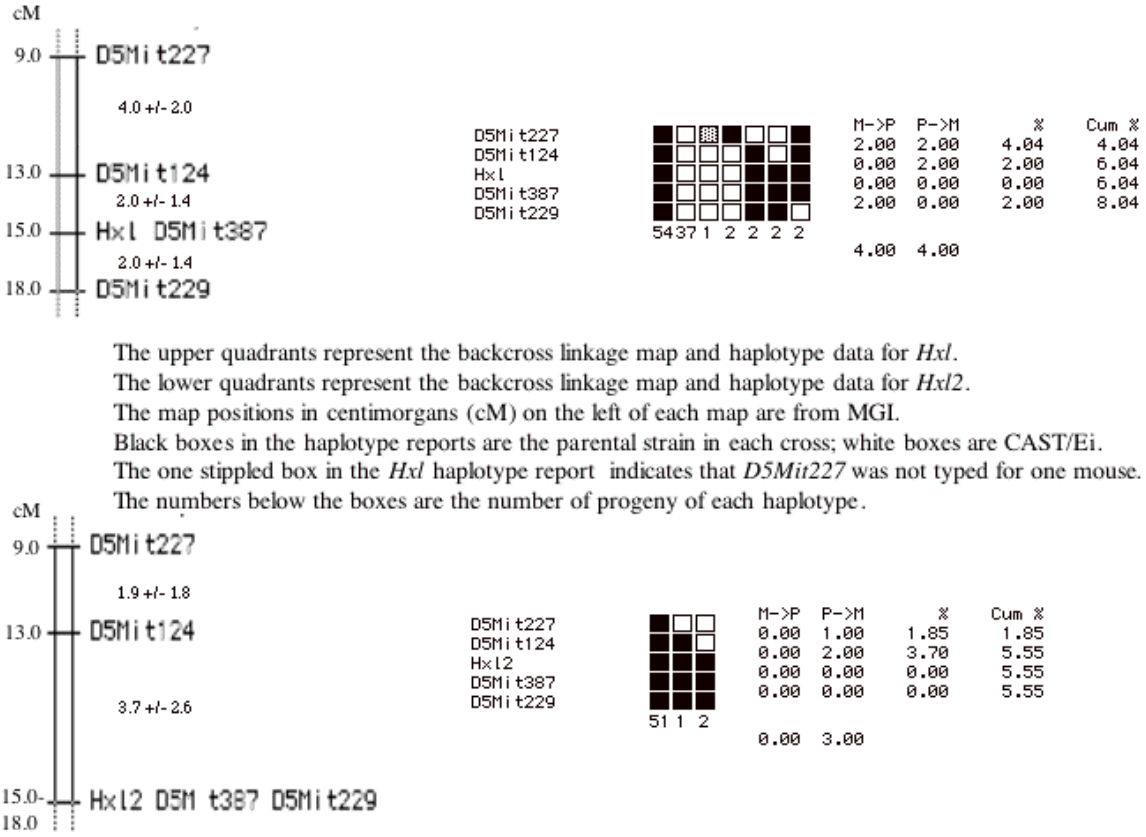
Phenotype categories: skeleton, limbs, toes

Abstract
One locus for dominant nonsyndromic preaxial polydactyly in humans is located within 7q36, which is homologous to the limb region 1 (*Lmbr1*) and hemimelic extra toes (*Hx*) segment of mouse Chromosome 5 (Clark et al 2001; OMIM). Based on appropriate map positions and similar phenotypes, we present two spontaneous mouse mutations that are putative remutations to *Hx* and are, hence, given *Hxl* and *Hxl2* as allele symbols.

Origin and Description
The *Hxl* allele was identified in 1996 as a phenotypic deviant in the B10.PL-$H2^{u}$(73NS)/Sn strain (Stock #000458) of the JMS facility of The Jackson Laboratory. The *Hxl2* allele was similarly identified in the B6129F1/J colony (Stock # 100492) in 1999. The *Hxl* mutation shows ~100% penetrance and is maintained on the original background by mating a heterozygote of either sex to a wildtype sibling. The *Hxl2* mutation also exhibits ~100% penetrance and is maintained similarly by brother x sister descendants of the original F1 mutant mouse. Homozygotes of each gender of both *Hxl* and *Hxl2* breed, but less readily than heterozygotes. Homozygotes of each mutation examined visibly and by alizarin staining seem phenotypically similar to heterozygote siblings which implies dominant inheritance on these backgrounds. Comparative skeletal morphometry to exclude semi-dominant inheritance was not done. DNA of both mutations has been cryopreserved in The Jackson Laboratory DNA Resource. Embryos from matings of C57BL/6J dams x *Hxl*/*Hxl* sires are cryopreserved as Stock #003561. Sperm samples from heterozygote males of each mutation are currently being cryopreserved.

Genetic Analysis
A male heterozygote of each mutation was mated to a CAST/Ei female. Affected F1 mice of both sexes of each mutation were mated to C57BL/6J wildtype. Individual N2 spleen tip DNAs were used in standard PCR reactions using MIT microsatellite markers. Both classes were typed in the *Hxl* cross, but only affected mice in the *Hxl2* cross as a small N indicated proximity to *Hxl*. We could not verify with the electrophoretic conditions whether *Hxl2* is of B6 or 129P origin. Linkage data for both crosses is available from

MGD; accession number J:83105. The order of the MIT markers used in these crosses was determined with Map Manager (Manly, 1993). Our mapping of *Hxl* and *Hxl2* (see figure below) agrees with the annotations of CDS, MGD, and MGSC. *Hxl* and *Hxl2* are located in the *Lmbr1* and *Hx* region of mouse Chromosome 5.



The upper quadrants represent the backcross linkage map and haplotype data for *Hxl*.
The lower quadrants represent the backcross linkage map and haplotype data for *Hxl2*.
The map positions in centimorgans (cM) on the left of each map are from MGI.
Black boxes in the haplotype reports are the parental strain in each cross; white boxes are CAST/Ei.
The one stippled box in the *Hxl* haplotype report indicates that *D5Mit227* was not typed for one mouse.
The numbers below the boxes are the number of progeny of each haplotype.

Acknowledgements
We thank Rebecca Coombs and Stacey Thomas for initial observations of the phenotypic deviants *Hxl* and *Hxl2*, respectively. We also thank Sandra Gray and Leigh Ann Kulla for colony assistance.

References

Clark RM, Marker PC, Roessler E, Dutra A, Schimenti JC, Muenke M, Kingsley DM. (2001). Reciprocal mouse and human limb phenotypes caused by gain-and loss-of-function affecting *lmbr1*. Genetics 159, 715-26.

MGD 2003, Mouse Genome Database, Mouse Genome Informatics Project, The Jackson Laboratory, Bar Harbor, ME. (www.informatics.jax.org)

MGSC12.3.1, Mouse Genome Sequencing Consortium (www.ensembl.org/Mus_musculus/)

Manley KF (1993) A MacIntosh program for storage and analysis of experimental mapping data. Mamm Genome 4, 303-3313.

OMIM 2003 Online Mendelian Inheritance in Man (http://omim.org)