Atypical hair loss; a new skin and hair mutation on Chromosome 6.

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Mutation (allele) symbol: *aphl*

Mutation (allele) name: atypical hair loss

Gene symbol: *aphl*

Strain of origin: MRL/MpJ-*Fas*^{lpr}/J

Current strain name: MRL/MpJ-*aphl*/GrsrJ

Stock #013782 (jaxmice.jax.org)

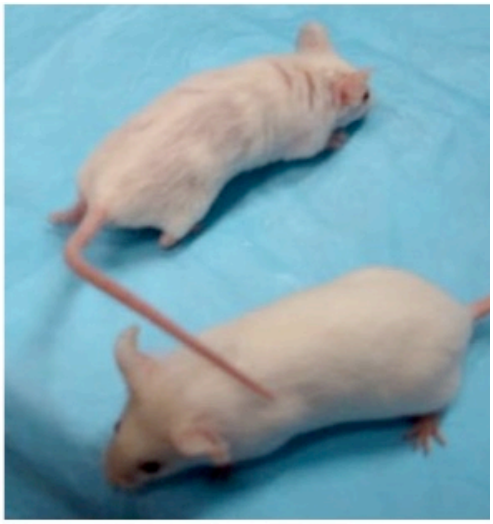
Phenotype categories: Skin and Hair

Origin and Description

The new recessively inherited atypical hair loss (*aphl*) mutation arose spontaneously and was found by Bonnie Williams in a production colony of MRL/MpJ-*Fas*^{lpr}/J mice at the Jackson Laboratory.

Mice homozygous for the *aphl* mutation have abnormal sparse hair growth early in age and can be recognized when their first coat of hair comes in at about 7~8 days of age. The fur grows in stripes with bald stripes in between.

As the *aphl* mutant mice reach adulthood, hair seems to grow on almost every part of the body, but the hair does not fill in completely compared to their unaffected littermates. Homozygous mice often have a mild crusty growth and rash around their eyes.
Both homozygous and heterozygous *aphl* mutant mice are viable and fertile.



A 9-week-old *aphl*/*aphl* mutant mouse is shown in the background with a littermate control in the foreground.

Genetic Analysis

Using our standard mapping procedures, an *aphl* homozygous mouse was mated to an unaffected A/J mouse. F1 hybrid mice from this mating were intercrossed and produced 55 F2 affected mice for linkage analysis.

The *aphl* mutation maps to Chromosome 6 and has been positioned between *D6Mit184* (NCBI 37 Position 53.2Mb) and *D6Mit4* (NCBI 37 Position 80.5Mb). There was no recombination with *D6Mit17* (NCBI 37 Position 71.0Mb) and *D6Mit16* (NCBI 37 Position 71.2Mb) in 50 meioses tested.

Pathology

A routine pathological screen[1] of two homozygous mice and a control mouse at 18 weeks of age, showed one of the homozygotes had many small muscle fibers in it's leg, which may be a variant of normal. The same mouse also had mild hydrocephalus. The other homozygote mouse had no lesions.

Hair was plucked and observed from at 5 week old *aphl* homozygote. The hair slides showed nothing significant or unusual and all four-hair types were present.

Auditory brain stem response (ABR)[2] testing in two homozygous mice and one control at17 weeks of age showed elevated thresholds. These results are probably due to the MRL background and not the *aphl* mutation. The MRL/MpJ strain has vestibular and hearing defects that cause age related hearing loss.

The eyes of two homozygous mice at 16 weeks of age appear clinically normal but an electroretinograph (ERG) test showed a low cone response.

Acknowledgements

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[1]**Standard Histology Protocol used in The Mouse Mutant Resource**

For fixation of tissues, mice were deeply anesthetized with tribromoethanol (avertin) until they no longer displayed a withdrawal reflex in the hind limbs and then perfused intracardially with Bouin's fixative following a flush of the vasculature with saline solution. After soaking in Bouin's for one week to demineralize bones, tissues were dissected. Six segments of spine with axial muscles and spinal cord in situ, representing cervical, thoracic and lumbar spinal segments, were dissected. The brain was removed and sliced into 6 cross sectional pieces at the levels of olfactory lobes, frontal cortex, striatum, thalamus, midbrain, rostral and caudal medulla with cerebellum. Midsagittal slices of hind leg through the knees were prepared. Slices of basal skull through the pituitary and inner ears were taken. Both eyes, salivary glands and submandibular lymph node, trachea plus thyroid and sometimes parathyroid were removed and cassetted. A longitudinal slice of skin from the back was removed. The thymus, slices of lung, and a longitudinal slice of heart were cassetted. Similarly slices of liver through gall bladder, kidney with adrenal attached, pancreas and spleen were prepared. The stomach was sliced longitudinally to include both squamous and glandular portions. Loops of small intestine from 3 levels and slices of large intestine and cecum were removed, as were slices of urinary bladder. The whole uterus, with ovaries attached, was taken. In males testes were sliced longitudinally. The accessory male organs including seminal vesicles, coagulating gland and prostate were removed en block. Altogether in most cases all tissue fit into a total of

10 cassettes. The cassettes were processed in an automatic tissue processor to dehydrate tissues which were then embedded in paraffin. Six micron sections were cut and stained with hematoxylin and eosin (H&E). Sections of brain and spinal cord in vertebral bones also were stained with luxol fast blue (LFB) for myelin and cresylecht violet (CV) for cellular detail.

[2]**ABR thresholds** in mice are determined using a semi-automated computer system (Intelligent Hearing Systems, Miami, Florida). Subdermal needle electrodes are inserted at the vertex and ventrolaterally to both ears of anesthetized mice. Specific auditory stimuli from 10-100 dB SPL are delivered binaurally through plastic tubes from high frequency transducers. ABR thresholds are obtained, in an acoustic chamber, for clicks and for 8, 16, and 32 kHz pure-tone pips.