Follicular dystrophy: a new skin and hair mutation on mouse Chromosome 2

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Mutation (allele) symbol: *Ass1*^{fold}

Mutation (allele) name: follicular dystrophy

Gene symbol: *Ass1*

Strain of origin: P/J

Current strain name: B6Ei.P-*Ass1*^{fold}/GrsrJ

Stock #006449 (jaxmice.jax.org)

Phenotype categories: skin and hair, size

Abstract
A new spontaneous autosomal recessive hair mutation named follicular dystrophy (*fold*) has been found at The Jackson Laboratory in a production colony of P/J mice. Mice homozygous for the *fold* mutation have a smaller body size than littermate controls and can be characterized by a lack of visible hair at one week of age and by wrinkled skin by two weeks of age. F2 progeny generated by a linkage cross to CAST/Ei were utilized to map the follicular dystrophy mutation to Chromosome 2.

Origin and Description
Throughout their relatively short lifespan, mice homozygous for the *fold* mutation have a body size that is smaller than normal littermates. Mutants of both sexes exhibit shortened lifespans; most die at three weeks of age and to date, no homozygote has lived long enough to breed. Hair is not visible by one week of age (see photo) but some hair does grow in to give the appearance of a sparse coat by weaning age at three weeks (see photo). At two weeks of age the skin is noticeably wrinkled.

A *fold*/*fold* mutant on the right and a control on the left. Both at 7 days of age.

A *fold*/*fold* mutant mouse on the left and a control on the right. Both at 2 weeks of age.

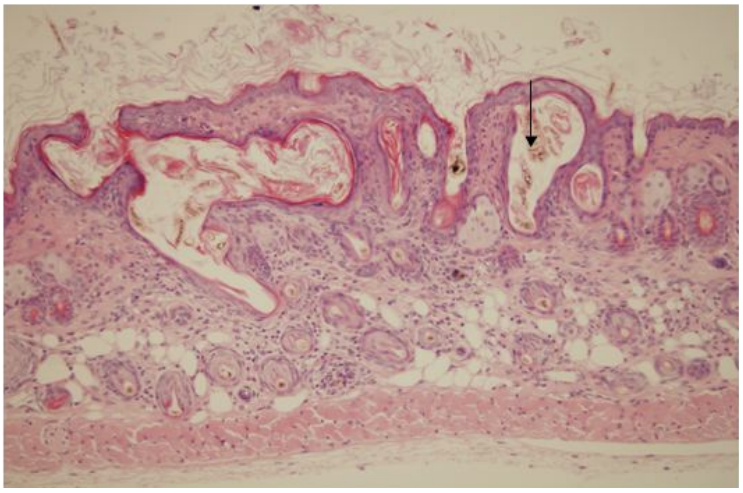
This colony is maintained by progeny testing to produce heterozygous pairs or by ovarian transplants performed on homozygous females, which then are mated to C57BL6/JEi males. The current generation is F73 + N4 to C57BL/6JEi .

Genetic Analysis

The recessive inheritance of the follicular dystrophy mutation was determined by mating a female CAST/Ei to a male heterozygote *fold*/+. This mating produced no mutants out of eleven progeny born in the F1 generation. Using our standard mapping protocols, an intercross of tested F1s from the previous mating did produce the mutant phenotype in the F2 generation confirming recessive inheritance. This intercross produced 52 F2 mutant progeny that were used to map *fold* to Chromosome 2. The *fold* mutation mapped between *D2Mit64* (NCBIm36 position 31.1 MB) and *D2Mit522* (position 32.7-32.9 MB).

Pathology

Eleven homozygous follicular dystrophy mice were sent to pathology for a routine pathological screen[1] and were found to have dermatitis and degeneration of the testis in one male. Others had dysplastic hair follicles (see photo). The follicular dystrophy seen was the hair follicle not producing a normal hair fiber.



Skin from a fold mutant showing dysplastic hair follicles (see arrow).

Hearing as assessed by Auditory Brainstem Response[2] testing of two homozygous *fold*/*fold* mice and one control littermate was normal.

Eyes of two mutants and controls were examined using an ophthalmoscope and found to have normal iris, lens and retinas.

Discussion

The new follicular dystrophy mutation maps near two similar skin and hair mutations, wrinkle-free (*Slc27a4*^{wrfr}) (NCBIm36 position 29.7 MB) and a targeted null mutation in the integrin beta 6 (*Itgb6*) gene (NCBIm36 position 60.3-60.5. However both of these genes are outside of the critical region for the *fold* mutation. To date no other skin and hair mutations are mapped to the *fold* region.

Additional Information: 11-9-2010- October issue of Am J Pathol, Perez et al. (v177 p1958) cloned *fold*. It is an allele of argininosuccinate synthetase 1, gene symbol *Ass1*.

Acknowledgements

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References

Casey L. Moulson, Daniel R. Martin, Jesse J. Lugus, Jean E. Schaffer, Anne C. Lind, and Jeffrey H. Miner. Cloning of wrinkle-free, a previously uncharacterized mouse mutation, reveals crucial roles for fatty acid transport protein 4 in skin and hair development. PNAS 2003 April 29; 100(9): 5274-9.

Protocols

[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.