Severe kyphosis (*sky*); a new skeletal mutation on Chromosome 14

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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: *sky*

Mutation (allele) name: severe kyphosis

Gene symbol: *sky*

Strain of origin: DBA/2J

Current strain name: DBA/2J-*sky*/J

Stock #006057 (jaxmice.jax.org)

Phenotype categories: skeleton/limbs

Abstract
A new spontaneous recessive mutation arose at the Jackson Laboratory and has been named severe kyphosis (*sky*). This new skeletal mutation maps to Chromosome 14.

Origin and Description
Mice displaying severe kyphosis were found by Marijo Vollmer in a production colony of DBA/2J mice at the Jackson Laboratory. Mice homozygous for the *sky* mutation have open eyelids at birth leading to injury and blindness, and exhibit a progressive S-shaped kyphosis of the lumbar region of the spine that becomes very severe. Mice homozygous for the *sky* mutation also display a shortened trunk due to the severe kyphosis and their tails appear to be in a higher position than normal. Homozygous mice generally die between 3 and 6 months of age, however some have lived longer than 6 months. Homozygotes do not breed.

Genetic Analysis
Using the standard mapping procedures of The Mouse Mutant Resource, a mouse homozygous for the *sky* mutation was mated to a C57BL/6J mouse. The normal looking F1 progeny from this cross were then intercrossed and produced 105 affected mice that were utilized for linkage analysis. The *sky* mutation maps to Chromosome 14 with only one recombinant in 50 meioses for *D14Mit10*, 3 recombinants in 24 meioses for *D14Mit50*, and 10 single recombinants and one double recombinant in 108 meioses for *D14Mit54*.

Pathology
Hearing as accessed by auditory brain stem response (ABR) testing of a mutant and control at one month of age, and two mutants at two months of age, reveals severe hearing loss in all mice tested. The hearing loss is due to the DBA/2J background strain, which has early onset age related hearing loss (AHL), and is not due to the *sky* mutation.

The eyes of one homozygous mutant and a control at 4 weeks of age were examined with

an ophthalmoscope. The homozygous mutant had a bad cornea, pupil, and iris. The cornea was vascular and the retina could not be seen.

A pathological screen[1] of a *sky*/*sky* mutant showed in sagittal serial sections of the spine only degeneration of articular cartilage, which may be nonspecific. A homozygous mouse at 3 weeks of age showed degeneration of spinal particular cartilage. There are small granulomas in muscle and brown fat. Serial cross sections of brain had no lesions. A homozygous mouse at 11 days of age showed hypotonic spine. In lateral serial sections there are foci of periarticular carticular necrosis. There are also foci of fat necrosis.

Acknowledgements
We thank Marijo Vollmer for discovery of the mutant, Rod Bronson and Coleen Marden for pathological screening, Chantal Longo-Guess for hearing assessment, Norm Hawes for the eye examinations.

[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.