Scrambler 4 Jackson; A new remutation to scrambler in the *Dab1* Gene

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Mutation (allele) symbol: *Dab1*$^{scm\text{-}4J}$

Mutation (allele) name: scrambler 4 Jackson

Gene symbol: *Dab1*

Strain of origin: CBA/J

Current strain name: CBA/J-*Dab1*$^{scm\text{-}4J}$/GrsrJ

Stock #010970 (jaxmice.jax.org)

Phenotype categories: neurological

Abstract
Scrambler 4 Jackson (*scm-4J*) is a recessive remutation located in the *Dab1* gene on Chromosome 4. Affected animals can be recognized by two weeks of age by their small size, tremor, and leaning side-to-side gait. Homozygotes may die by three weeks of age but most live to adulthood.

Origin and Description
The scrambler 4 Jackson remutation was found at The Jackson Laboratory by Kimberly Hatch in a production colony of CBA/J mice in 2006. A mouse affected by this remutation was first recognized by its small size and shaky walk. The leaning phenotype is also striking as seen when affected mice try to run around their cage to keep up with unaffected littermates. The littermate controls are normal in size and actions. The colony of *scm-4J* mice is maintained by progeny test and tested heterozygotes are normal.

Genetic Analysis
This recessive mutation and was proven to be allelic with *Dab1*^{scm} using a direct test for allelism. Heterozygous matings of *Dab1*$^{scm\text{-}2J}$ to heterozygotes of this new remutation, scrambler 4 Jackson, produced three affected mice out of twenty progeny born, proving allelism.

Pathology
Our standard pathology screen[1] of two *scm-4J* homozygotes found poor marrow, thymic atrophy and disorganiztion of neurons in the brain, consistent with scrambler mutations lesions. Two tested control mice were normal. All mice screened had retinal degeneration 1 (*Pde6b*^{rd1}) which is a CBA/J background strain characteristic and not caused by this new remutation. Hearing as assessed by audiotory brainstem response testing on two homozygote *scm-4J* mice and two control animals showed normal hearing.

Discussion

We report a remutation on Chromosome 4 having pathology similar to the original scrambler mutation *Dab1*^{scm}.

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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.