Purkinje cell degeneration 8 Jackson

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Mutation (allele) symbol: *Agtpbp1*$^{pcd\text{-}8J}$

Mutation (allele) name: Purkinje cell degeneration 8 Jackson

Gene symbol: *Agtpbp1*

Strain of origin: BALB/cJ

Current strain name: BALB/cJ-*Agtpbp1*$^{pcd\text{-}8J}$/GrsrJ

Stock #008292 **NOTE**: As of March 30, 2009 available as DNA only from the Jackson Laboratory DNA Resource

Phenotype categories: Neurological

Origin and Description

The neurological recessive *Agtpbp1*$^{pcd\text{-}8J}$ mutation arose spontaneously and was discovered by Teresa Torrey in a production colony of BALB/cJ mice at the Jackson Laboratory. Like the original Purkinje cell degeneration (*pcd*) mice, *Agtpbp1*$^{pcd\text{-}8J}$ mice are recognized by a moderate ataxia at 3-4 weeks of age. Homozygous mutant mice are smaller than littermates, present the severe deficiency of Purkinje cells characteristic of other *Agtpbp1* alleles and live through adulthood. Homozygous females are fertile but are very poor breeders. Males do not breed.

Genetic Analysis

Using our standard mapping protocols[1], a mutant mouse affected with the *Agtpbp1*$^{pcd\text{-}8J}$ mutation was mated to a CAST/EiJ mouse. No affected F1 mice were observed in the progeny produced by this mating. The F1 mice were then intercrossed and generated 41 affected F2 mice of which 23 were used for linkage analysis. The *Agtpbp1*$^{pcd\text{-}8J}$ mutation maps to Chromosome 13, proximal to *D13Mit143* (NCBI 36 position 73.7Mb), and is non-recombinant with *D13Mit157* (NCBI 36 position 60.0 mb) and *D13Mit311* (NCBI 36 position 63.6 mb). Based on the chromosomal position from our initial mapping data and the phenotypic similarities with the original *pcd* mutants, a direct test for allelism was set up by mating 2 female mice heterozygous for this new mutation to a heterozygous male *Agtpbp1*$^{pcd\text{-}3J}$ mouse. This mating produced 13 pups of which 2 were affected with the mutant phenotype, proving allelism.

Pathology

A routine pathological screen[1] of one female homozygous *Agtpbp1*$^{pcd\text{-}8J}$ mouse showed loss of Purkinje cells and had retinal degeneration at 7 weeks of age. One male

homozygous mouse showed no Purkinje cells, but had retinal degeneration and abnormal sperm at 19 weeks of age. Auditory-evoked brain stem response[2] (ABR) testing of one homozygous mouse at 6 weeks of age revealed no hearing loss. Electroretinogram testing (ERG) of the eyes of one homozygous male showed low rod and cone at 6 weeks of age. One female mouse homozygous for the *Agtpbp1*$^{pcd\text{-}8J}$ was also examined at 4 months of age and showed thin retinal vessels.

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]Auditory-Evoked Brainstem Response (ABR) Thresholds

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. ABR thresholds of all mice and strains tested are entered in spreadsheet files for storage, easy access, and for the production of periodic progress reports. Click-evoked ABR waveforms, obtained at threshold (T) and at T+10, T+20 and T+30 dB or each mouse, are also stored for future reference. Mice of the CBA/CaJ strain are tested periodically as references for normal hearing, and for monitoring the reliability of the equipment and testing procedures.