A collaboration of scientists from the Veterinary Neurological Center in Los Vegas, the University of Missouri-Columbia (UMC), the University of California-San Diego, and Cornell University in Ithaca has recently described a new form of NCL in American Bulldogs. At UMC we have been studying DNA from affected American Bulldogs and their relatives, and have discovered the mutation causing NCL in this breed. A DNA test is now available which will definitively identify clear, carrier, and affected dogs. The charge for this test is $40 per dog, payable to "University of Missouri". For instructions and forms, see the SAMPLE SUBMISSION section of the NCL portion of www.CanineGeneticDiseases.net .

NCL Description for American Bulldogs

Age of onset of clinical signs: 0.9 to 3 years

Age of death or euthanasia: 3.5 to 5.5 years

Abnormalities often observed by the owner:
***Mental changes*:** Physical symptoms may appear to worsen during times of stress. Affected dogs do not indicate they are in any pain as coordination decreases.
***Changes in gait and posture*:** Initially, uncoordinated movement in the rear is noted. As the disease progresses, affected dogs develop a wide-based stance in the rear, and eventually involving all four legs. Affected dogs may exhibit muscle twitching, especially when sleeping. The dogs remain well-muscled through the course of the disease.
***Visual abnormalities*:** None reported
Seizures/convulsions: None reported
Other changes: None reported

Abnormalities observed upon clinical examinations:
Clinical neurologic changes: Progressive ataxia and hypermetria is present in all four limbs but more pronounced in the pelvic limbs. Conscious proprioception and hopping reactions are delayed in the pelvic limbs but normal in the forelimbs on initial examination. In advanced stages conscious proprioception reactions are absent in all four limbs and dogs have difficulty rising from a recumbent position without assistance. A wide-based stance of the pelvic limbs is observed in younger affected dogs; this progresses to a wide-based stance of all four limbs at later examinations. Spinal reflexes and cranial nerve examinations are normal. The dogs remain well muscled.
***Clinical ophthalmic changes*:** None reported
***Visual abnormalities*:** None reported
***Retinal changes*:** None reported
Electroretinography (ERG): None reported
***Other clinical findings*:** None reported

Histopathology
***Brain*:** The entire external surface of the brain has a light brown hue but no evidence of cortical atrophy. Microscopically, PAS-positive storage material is present in cerebral cortex, brainstem, and cerebellum. The storage material in all cells exhibits a golden-yellow autofluorescence. Axonal spheroids are present in the brain and spinal cord. Ultrastructurally, storage bodies consist of membrane-bound organelles with cross-sectional diameters generally ranging from 0.5 to 3 microns. The inclusion body profiles

are sometimes round but more often irregular. The bulk of the storage body contents are coarsely granular and most storage bodies contain numbers of somewhat spherical aggregates of the granular material. In addition, storage bodies from all 3 cell types contain well-delineated spherical dark-staining inclusions that are mostly smaller than 0.1 microns in diameter. In some cells in and near the Purkinje cell layer of the cerebellum, the perinuclear cytoplasm is filled with storage material that appears to be an aggregation of smaller storage bodies that have fused.
Eyes: Microscopically, PAS-positive storage material is present in ganglion cells of the retina. Under electron microscopic examination, the storage bodies in retinal ganglion cells have an additional ultrastructural feature of lighter-staining spherical inclusions with the relatively uniform electron density typical of lipid droplets.
***Other organs and structures*:** None noted

Mode of inheritance: Autosomal recessive.

Gene containing mutation: The causative mutation has been identified and a DNA test is now available. See details above.

References:
Evans J, Katz ML, Levesque D, Shelton D, deLahunta A and O'Brien DP: A Variant Form of Neuronal Ceroid Lipofuscinosis in American Bulldogs*. J. Vet. Internal Med.,* 19:44-51, 2005.