

**Grant:** 0732: *Identification of Mutations Responsible for Hereditary Neurodegenerative Disorders in Dogs*

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**Report to Grant Sponsor:** (Lay Abstract allowed to be reproduced)

From PI:

Both humans and dogs suffer from a large number of inherited disorders that lead to degenerative changes of the central nervous system. These diseases can cause such symptoms as visual impairment, loss of coordination, seizures, declines in cognitive function, paralysis, and ultimately death. Among these inherited neurodegenerative disorders are the neuronal ceroid lipofuscinoses (NCLs) and degenerative myelopathy (DM). NCLs and DM have been reported in a large number of dog breeds. To date, mutations in at least 8 different genes have been found to cause NCL in children. Dogs have versions of most of the genes present in humans. We previously have found the mutations in 3 genes that cause NCL in dogs: the CLN8 gene in English Setters, the CTSD gene in American Bulldogs, and the TPP1 gene in Dachshunds. We currently offer DNA tests for these mutations. Unfortunately, it appears that each NCL mutation is unique to a specific breed, and in fact more than one NCL mutation can occur in the same breed. Therefore, research must be done to identify the NCL mutation for each breed in which it occurs. We recently identified two new NCL mutations in dogs: a mutation in the CLN6 gene in Australian Shepherds and a CLN1 mutation in Dachshunds. Tests for both of these mutations will soon be made available. A primary focus of our current research is to identify the mutations that cause as many forms of canine NCL as possible and to offer these tests at as low a cost as possible. Over the past 6 months, most of our work on the canine NCLs has been focused on the forms of the disease that occur in Tibetan Terriers, Dachshunds and Australian Shepherds. If you have an Australian Shepherd or a Dachshund that is exhibiting symptoms of NCL or a dog closely related to the affected animal, please send us a blood sample and we will test for the appropriate mutation at no charge. Tibetan Terriers suffer from a late-onset form of NCL in which the symptoms usually do not become apparent until the dog is more than 5 years old. As reported previously, we have identified the chromosome on which the Tibetan Terrier NCL gene is located. The location of this gene indicates that it is a gene that has not previously been associated with NCL in either dogs or humans. We are working to narrow down the precise location of the NCL gene in this breed so that we can determine its identity. We are still collecting samples from affected Tibetan Terriers and unaffected dogs of this breed that are over 10 years old. For these and other breeds, breed-specific descriptions of NCL symptoms in many breeds can be found at our website ([http://www.caninegeneticdiseases.net/CL\\_site/mainCL.htm](http://www.caninegeneticdiseases.net/CL_site/mainCL.htm)). If your dog exhibits a pattern of symptoms consistent with NCL, regardless of breed, we urge you to consult with your veterinarian and a neurology specialist if necessary. If other causes of the symptoms can be ruled out, we ask that you contact us as instructed on our website. For English Setters, American Bulldogs, Dachshunds, and Australian Shepherds with the appropriate symptoms, we will ask for a blood sample on which we can perform the DNA test for NCL. For all other breeds, we will request a blood sample and health and pedigree information (all information on specific dogs is kept confidential). We will use this sample and information to look for the NCL mutation in your breed. Our goal is to give every breed the tools necessary to screen for and eliminate NCL and other inherited neurodegenerative diseases.

Meanwhile, if you have an affected dog that is going to be euthanized and are willing to donate tissues, please contact us.