

**Progress Report to the  
Tibetan Terrier Club of America  
Tibetan Terrier Neuronal Ceroid  
Lipofuscinosis Research  
June, 2007**

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A major focus of our research continues to be to identify the mutation responsible for neuronal ceroid lipofuscinosis (NCL) in Tibetan Terriers. (A mutation is a small defect in the genetic code). Tibetan Terrier NCL is a progressive inherited neurodegenerative disease with an autosomal recessive pattern of transmission. The term autosomal refers to the fact that both sexes are equally likely to be affected. If a disease has a recessive pattern of inheritance, affected dogs can arise from mating between either 2 affected dogs, one affected and one unaffected (carrier) dog, or between 2 unaffected (carrier) dogs. The disease has a relatively late onset, with symptoms typically not becoming apparent until 5 to 7 years of age. Affected dogs exhibit personality changes, vision impairment, loss of physical coordination, and often have seizures in the late stages of the disease. The late onset makes it very difficult to eradicate the disease by selective breeding based on disease symptoms alone. This makes it important that a DNA test for the mutation be developed so that affected dogs and carriers can be identified prior to breeding. To develop such a test, we first need to find the disease mutation. This requires that we obtain DNA samples from a large number of Tibetan Terriers with NCL and from clearly unaffected Tibetan Terriers. We have developed a system for identifying potentially affected dogs and of confirming a diagnosis of NCL via postmortem examination of brain and retinal tissues for the presence of disease-specific storage material. If dogs begin to exhibit changes in behavior and personality after about 4 years of age, we ask that the owners contact us, complete a questionnaire that includes relevant health and behavior information, provide us with a pedigree, and send us a blood sample for DNA extraction. Instructions for submitting samples and a copy of the questionnaire can be found on our website ([http://www.caninegeneticdiseases.net/CL\\_site/mainCL.htm](http://www.caninegeneticdiseases.net/CL_site/mainCL.htm)). Based on the information on the questionnaire, we can usually say with about 80%

certainty whether a dog has NCL. Collection of samples and symptom information from hundreds of Tibetan Terriers over a number of years has resulted in confirmed diagnoses of over 30 cases of NCL in this breed. Based on the symptoms that were reported in these dogs prior to euthanasia, a pattern of symptoms has emerged that is reliably diagnostic. Thus, we can usually tell from the answers to our questionnaire whether a dog is likely to be suffering from NCL. We have been notified of several Tibetan Terriers that were exhibiting some of the signs of NCL, but with some important differences. When tissues from these dogs were examined postmortem, we confirmed that they did not suffer from NCL. Confirming that these dogs were negative for the disease gives us confidence in our ability to make the diagnosis based on the questionnaire alone. However, because some other condition could potentially mimic NCL, we still require postmortem confirmation of disease status for dogs to be included in our initial search for the disease gene. We currently continue to receive samples and identify affected dogs.

In our search for the disease gene, it is also important that we obtain blood samples and health information from Tibetan Terriers that are NOT suffering from NCL. We would like to obtain blood samples from dogs that are at least 10 years of age and have not shown any behavioral abnormalities. Please contact us if you have dogs that you would like to enter into the study. In our search for the Tibetan Terrier NCL mutation, we have now narrowed down the location of this mutation to a small region of one of the dogs' chromosomes. There are many different genes in this region that could harbor the disease mutation. We are currently analyzing these genes to determine which of them is abnormal in Tibetan Terriers with NCL. Once we find the abnormality, we will be able to devise a test for it that can be performed using a blood sample from dogs of any age.

## Canine Neuronal Ceroid Lipofuscinosis

This website is designed to provide basic information on canine ceroid lipofuscinosis (neuronal ceroid lipofuscinosis), and serve as a resource for those concerned with this disease: breeders, owners, veterinarians, and researchers.

Information presented here is not a substitute for an accurate diagnosis and specific advice geared to your pet's needs. If you suspect your dog has neuronal ceroid lipofuscinosis, we encourage you to have a veterinarian or veterinary neurologist examine the dog and advise you.

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### **\*\*TIBETAN TERRIER SAMPLES URGENTLY NEEDED!\*\***

To help us find the mutation responsible for NCL in Tibetan Terriers, we need blood samples from any healthy Tibetans who are at least 8 years of age and have shown no signs of NCL. We also need additional samples from dogs who may be affected with NCL. If you are able to assist with this research by providing samples, please [contact us](#) or follow the instructions in [SAMPLE SUBMISSION](#).

A voluntary registry of Tibetan Terriers that were confirmed to be affected with NCL can be found at the [website linked here](#). Samples from relatives of these dogs would be particularly useful in finding the Tibetan Terrier NCL mutation.

Notice posted 11-10-2005, updated 12-08-05

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### **DNA TEST NOW AVAILABLE FOR DACHSHUNDS**

Dachshund owners please see further information in the breed listing portion of the [BASICS](#) section, and use instructions and forms available in the [SAMPLE SUBMISSION](#) section to send samples.

## DNA TEST NOW AVAILABLE FOR AMERICAN BULLDOGS

American Bulldog owners please see further information in the breed listing portion of the [BASICS](#) section, and use instructions and forms available in the [SAMPLE SUBMISSION](#) section to send samples.

## DNA TEST NOW AVAILABLE FOR ENGLISH SETTERS

English Setter owners please see further information in the breed listing portion of the [BASICS](#) section, and use instructions and forms available in the [SAMPLE SUBMISSION](#) section to send samples.

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