Neuronal Ceroid Lipofuscinosis in Polish Lowland Sheepdogs (PONs)

The neuronal ceroid lipofuscinoses (NCLs) are inherited diseases in both people and dogs that cause progressive degeneration of the brain and usually the retina as well. This can result in loss of mental ability, movement abnormalities, personality changes, vision impairment, and seizures. Almost all of the NCLs are progressive. Affected people and dogs usually seem normal early in life, but once symptoms begin to appear, they get worse over time. Ultimately the NCLs are fatal in most people, usually during childhood, and lead to the need for euthanasia in dogs.

In people mutations in at least 14 different genes cause different forms of NCL. The different forms are given the short-hand names CLN1, CLN2, … up CLN14. Corresponding forms of all of these genes are present in dogs and mutations in any of these genes can cause canine NCL. NCL has been reported on the basis of symptoms in many dog breeds, including PON dogs. To date the genetic basis of these different forms of canine NCL have been traced to 8 different mutations. These are summarized in the table below.

Breed	Gene Containing NCL Mutation
Dachshund	CLN1
Dachshund	CLN2
English Setter	CLN8
American Bulldog	CLN10
Australian Shepherd	CLN6
Australian Shepherd	CLN8
Tibetan Terrier	CLN12
Chinese Crested	CLN7
Border Collie	CLN5

Each canine NCL mutation is specific to the breed in which it has been found. For example, the CLN7 mutation that causes NCL in Chinese Crested dogs has not been associated with NCL in any other breed. Even when two breeds have NCL resulting from mutations in the same gene (e.g. English Setters and Australian Shepherds with NCL both have CLN8 mutations), the specific mutations within that gene are different for the different breeds. What this means is that if we document NCL in a new breed, it will be fruitless to evaluate that breed for the known canine NCL mutations; a new mutation must be identified that is the cause of NCL in the new breed.

Until the disease-causing mutation is found in a dog breed, the only way to make a definitive diagnosis of NCL is to examine brain and retina tissues after death for pathological changes that are specific to the NCLs. If a dog exhibiting symptoms suggestive of NCL is euthanized, a DNA sample (usually from blood) is collected and the tissues are examined to make the diagnosis. If a positive diagnosis is made, The University of Missouri

Neurodegenerative Diseases Laboratory (NDRL) will examine the DNA to find the disease-causing mutation. Once we find the mutation, we can quickly develop a simple DNA test that uses cheek swab samples to distinguish dogs of that breed that are affected, carriers, or normal.

To date NCL has been confirmed by postmortem examination in a number of PON dogs from Europe, but we have not received DNA from any of these dogs and the genetic basis of NCL in this breed remains unknown. Based on symptoms, it appears that there may be 2 different forms of NCL in PON dogs – one form with in which symptoms first appear at about 6 months of age and another form in which symptoms do not appear until the dogs are 3 to 4 years old. In both forms symptoms can include some or all of the following: aggressive behavior, dementia, loss of coordination, vision difficulties, nervousness, personality changes, and in the later stages of disease, seizures. If your PON dog is exhibiting some of these symptoms and the symptoms get worse over time, a diagnosis of NCL should be considered. MRI can be performed to rule out some other potential causes, but it is not diagnostic for NCL. Unfortunately, no effective treatment exists for any of the known forms of NCL.

If you suspect that your PON may be suffering from NCL, please contact Professor Martin Katz of the NDRL at katzm@health.missouri.edu. He will ask that you complete a questionnaire about your dog's symptoms and that you provide him with a blood sample. If the point comes that your dog has to be euthanized, he will ask that your veterinarian provide him with the tissues required to make the diagnosis. If a positive diagnosis is made on even one PON from which we have obtained a blood sample, we will be able to find the disease-causing mutation and develop a test for it. While this will not help your dog directly, it will enable PON breeders to screen their dogs for the mutation before breeding and thus avoid breeding dogs that could produce affected puppies.

If you would like more information about canine NCL or have questions relating to your own dog, feel free to contact Professor Katz via e-mail.