



Canine Genetics Progress Report

Breed: Large Munsterlander

Condition: Hereditary Cataract

Date: 27.10.2008

Recent / Current Funding:

Funding Body: Kennel Club Charitable Trust

Amount: £250,000

Start Date: 01.03.2006, duration 36 months

The above grant is specifically to study Hereditary Cataract (HC) and Progressive Retinal Atrophy (PRA) in the Golden Retriever, the Tibetan Spaniel and the American Cocker Spaniel but it is our intention to also study any breeds for which we can collect sufficient samples.

In addition to the above personal donations of approximately £2000 have been received during 2008 to contribute to Hereditary Cataract research in the Large Munsterlander.

Sample Collection

Sample Collection has progressed well over the past year, although there have only been 3 new submissions since the last report. We have now collected DNA samples from 130 Large Munsterlanders. Of these samples 17 are from dogs with inherited cataracts. We also have samples from several dogs with opacities of the lens, but not necessarily inherited forms. These samples from dogs with slightly unusual forms of cataract will contribute to the later stages of the research, and will help understand which forms of cataract are inherited, but they will be classed as 'unknown' (as opposed to affected or unaffected) for the early stages of the research. The sample collection includes samples from many of the parents and littermates of affected dogs, which adds considerable strength to the sample collection.

The Large Munsterlander DNA sample collection is among the best that the AHT currently holds, in terms of the numbers of samples from affected dogs, and the large proportion of samples for which eye report information has been submitted. We do now have the minimum number of samples from affected dogs that are required to initiate DNA studies, but we encourage owners to continue to submit samples from both affected and unaffected sample to this research.

Studies In Other Breeds

The AHT has initiated DNA analyses of other breeds with HC, for which substantial sample collections already exist at the AHT. We have had some preliminary results that indicate at least one chromosome that is associated with HC

in Golden retrievers. We are calling this the *Golden Retriever HC chromosome*. Since the last report we have genotyped DNA from affected and unaffected Large Munsterlanders with genetic markers located along the *Golden Retriever HC chromosome*. If the Large Munsterlanders shared the Golden Retriever HC mutation we would also expect them to share DNA close to the mutation. Unfortunately this does not seem to be the case. The version of the HC chromosome that is shared between all HC affected Golden Retrievers is very different from the versions of the same chromosome we see in the affected Large Munsterlanders, and in contrast to the affected Golden retrievers, all of whom share at least one copy of the *HC chromosome*, the affected Large Munsterlanders do not all carry the same version of this chromosome. This has enabled us to conclude that the Large Munsterlanders and the Golden Retrievers do not share the HC mutation that is located on the *Golden Retriever HC chromosome*.

This means we will now progress to undertake a Whole Genome Scan (WGS) with Large Munsterlander DNA, to identify their '*HC chromosome*'. We have selected 17 dogs that are affected with cataracts that are typical of HC in the Large Munsterlander. The average age of diagnosis of these dogs was 3.00 years of age. We have also selected 29 dogs that were clear of cataracts at their last eye examination to act as our controls. These dogs had an average age at diagnosis of 6.69 years of age. DNA from these 36 dogs will be genotyped with 22,000 markers each in our initial WGS experiments. The Large Munsterlander samples will be genotyped alongside a large number of samples of other breeds with different conditions, and all samples will be prepared and genotyped at the same time. This means that the rate of progress of this stage of the project will be partly dependent on the speed with which we can get this large number of samples ready. But once the samples have been prepared and submitted for genotyping the data should be available fairly quickly.

In the previous reported we noted that the DNA yield from the Large Munsterlanders had been lower in general than for other breeds we are studying. As we have extracted DNA from many dogs now, all from swabs taken by many different owners, it is unlikely it is an 'owner-specific' effect and is more likely to be a breed-specific effect (perhaps Large Munsterlanders produce more or less saliva than other breeds, or are simply more active and dislike having swabs taken!).

Now we know that we need to progress to a whole-genome scan we may need more DNA from the 36 dogs we plan to genotype, and will therefore be contacting these owners within the next week or two to request additional DNA samples from their dogs; this will ensure we have sufficient DNA to conclude the studies. This by no means implies that the DNA samples we already have are not going to be useful, nor will they lead to inaccurate result; we are merely trying to ensure we have sufficient DNA from all the crucial dogs to ensure success.

Thank You

The AHT would like to thank the very many Munsterlander owners and breeders who have offered us samples and information about their dogs. Without this kind of co-operation we would not be in a position to investigate HC in this breed; with your continued co-operation we will continue to make progress.

We would also like to thank everybody who has raised and donated money for the research effort at the Animal Health Trust. As a charity we rely heavily on donations and they really do make a significant difference to the work we can do.