



Canine Genetics Progress Report

Breed: Lancashire Heelers and Miniature Bull Terriers

Condition: Primary Lens Luxation (PLL)

Date: 01.01.2008

Recent / Current Funding:

- Funding Body:* Kennel Club Health Foundation Fund

Amount: £83,281 (including £8000 from Miniature Bull Terrier Breed Club)
this grant was to study four inherited conditions, one of which was PLL

Start Date: March '03, 24 months
- Funding Body:* Kennel Club Health Foundation Fund

Amount: £49,823 (including £2000 from Lancashire Heeler Breed Club)

Start Date: March '05, 24 months
- Funding Body:* Canine Health Foundation (American Kennel Club)

Amount: \$9586

Start Date: January '05, 12 months
- Funding Body:* Canine Health Foundation (American Kennel Club)

Amount: \$12927

Start Date: February '07, 12 months
- Funding Body:* Miniature Bull Terrier Club

Amount: £12,000

Start Date: February '08, 12 months

The Primary Lens Luxation research project is currently collaboration between Cathryn Mellersh (AHT), David Sargan (University of Cambridge) and David Gould (Davies Veterinary Specialists).

Progress Update

As we have reported previously, considerable progress has been made recently to identify the region of the genome that contains the mutation responsible for PLL. We have identified a region, on chromosome 3, that is shared between all dogs that are affected with PLL. Slowly but surely we have been narrowing the region and now have reduced it to around 300,000 nucleotides or letters of DNA, which is less than a tenth of 1% of the canine genome. This is called the 'PLL critical region'

We have identified a gene within the critical region that is a very good candidate for PLL that we would now like to sequence (i.e. read letter by letter). Unfortunately the sequence and structure of the DNA in this region makes it technically challenging to sequence and this has meant that our progress with this gene has been slower than it would be for other, more normal, regions of the genome. We are about to undertake some experiments to measure the overall length of the gene in affected and unaffected dogs, to determine if a gross alteration in the length is causing the disease. If these studies provide evidence the gene is involved we will perform additional experiments to isolate the difficult region and finally sequence it, letter by letter, to identify the precise mutation.

We have also started to explore the possibility of developing a 'linkage-based' DNA test that would use the DNA within the PLL critical region to determine whether dogs are affected, carrier or clear of PLL. Because linkage-based tests do not assay for the presence or absence of the causal mutation, but rather rely on nearby 'linked' DNA, they are not 100% accurate, but if carefully designed they can achieve levels of accuracy in excess of 95% and would represent a useful tool with which breeders can start to reduce the incidence of this condition until the mutation itself is identified.

We have had a dedicated member of staff working on this project, and the principal investigators meet on a regular basis, to monitor progress and discuss results. Identifying the mutation responsible for this condition continues to be a major focus for all concerned with this project.

Sample Collection

The research has progressed sufficiently well that we are now only targeting samples from dogs, of any breed, that are *affected with PLL*. Samples from additional affected dogs will continue to play a

valuable role in the research right up until the point at which we find the mutation and can develop a DNA test.

We would also like to thank everybody who has made a financial donation to support our research studies and we are particularly grateful to the Miniature Bull Terrier Club for their very generous recent donation. As a charity the AHT relies heavily on donations, whilst all research performed at the University of Cambridge is also funded solely through external donations and competitive grants, and not through support from the higher education funding system. All donations to support our research are truly appreciated by both organisations.