Miniature & Bull Terrier Complaint and Genealogy (mBTcg)

Health - English Only => Eye issues => Topic started by: ChaosEnergy on April 21, 2008, 12:45:42 PM

Title: **AHT: Canine Genetics Progress Report Jul 2007**
Post by: **ChaosEnergy** on **April 21, 2008, 12:45:42 PM**

Source: http://www.lancashireheelers.org/AHTupdate01.php

Breed: Lancashire Heelers
Condition: Primary Lens Luxation (PLL)
Date: 01.07.2007

Recent / Current Funding:

1. 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

2. Funding Body: Kennel Club Health Foundation Fund
Amount: £49,823 (including £2000 from Lancashire Heeler Breed Club) Start Date: March '05, 24 months

3. Funding Body: Canine Health Foundation (American Kennel Club)
Amount: $9586
Start Date: January '05, 12 months

4. Funding Body: Canine Health Foundation (American Kennel Club)
Amount: $12927
Start Date: February '07, 12 months

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

Progress Update
The PLL research has progressed very well over the last 12 months. Approximately a year ago, working primarily with DNA samples from Lancashire Heelers and Miniature Bull Terriers, we identified a small region of a single chromosome where the PLL mutation is located. The dog has 38 chromosomes, so this result represented a significant step forward as it meant we had narrowed our search for the mutation to around 1-2% of the canine genome. However, it should be noted that the region still contained several million nucleotides or `letters' of DNA, the equivalent to 2 or 3 inch-thick text books, so there was still a considerable amount of DNA in the region under consideration. The problem is complicated because these DNA texts are written in a way that allows several thousand changes over this region between each individual (giving them their individual identities), but we are looking for a single change that is shared by all luxating individuals, but not by unaffected individuals. The region we have identified is referred to as the `PLL critical region'.
Further analysis of samples from other breeds indicated the same region of the

same chromosome was also associated with PLL in other breeds, including the Tibetan Terrier and the Jack Russell Terrier.
We have examined several genes in detail that are located within the PLL critical region and that seemed good candidates for the condition and have excluded them all from involvement in the development of PLL.
Sequencing experiments (i.e. experiments to `read' DNA letter by letter) are expensive and time-consuming and we have decided that before we undertake further sequencing we will attempt to narrow the PLL critical region further, so we have even less DNA to hunt through to find the actual mutation that is responsible for PLL in all the breeds we are studying. To do this we are analysing a large number of genetic markers, located very close together, in samples of dogs of many different breeds that are all affected with PLL.
These experiments are still underway, but recently we have had results that have enabled us to narrow the region to a mere 600,000 nucleotides of DNA, which is around 0.025% of the canine genome; a tiny fraction. These experiments are still ongoing but by the time they are finished we hope to be left with a very region of DNA that is small enough for us to sequence, nucleotide by nucleotide, until we find the mutation.
Sample Collection
Sample collection continues to go very well and the Lancashire Heeler owners and breeders should be congratulated on their efforts to collect samples for this project. We now have DNA samples from 421 Heelers stored at the AHT, of which 51 are reported to be affected with PLL. The research has progressed sufficiently well that we are no longer collecting samples from `any' Heelers, but rather are targeting only those 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. 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.