



Canine Genetics Research Progress Report

Breed: Keeshond

Condition: Idiopathic Epilepsy

Date: May 2014

Current Funding:

Funding Body: Kennel Club Charitable Trust

This grant has now expired

The Animal Health Trust (AHT) staff members involved in investigating idiopathic epilepsy in the Keeshond are generously supported by the Kennel Club, as part of the Kennel Club Genetics Centre at the AHT. The whole genome scan, including laboratory reagents and consumables required to prepare DNA samples for processing, has been funded by the Kennel Club Charitable Trust.

What stage are we at with this research?

Scientists at the AHT, alongside Dr Barbara Skelly from the University of Cambridge, have conducted an updated genome-wide association study (genome scan) in the Keeshond to search for regions of the DNA that might be involved in idiopathic epilepsy, as there is currently no DNA-based diagnostic test for idiopathic epilepsy in the Keeshond. This report summarises the results of our investigations and suggests future directions.

What did the whole genome scan involve?

As previously, we compared thousands of DNA markers in Keeshonds with epilepsy (cases) with those in Keeshonds free of seizures (controls) to look for regions in the genome that are consistently shared among cases, but that are different in the controls. Since our work

in 2013, we have had 18 new epilepsy cases submitted, and these were reviewed by Dr Barbara Skelly to confirm their clinical diagnosis. Sixteen of these cases had sufficient diagnostic information to enable their designation as robust cases, and the remaining two cases were less well-defined. We have had 60 new controls submitted since 2013 that were aged eight years or over and free of seizures at the time of sample submission, and these were representative of the countries that the cases were from.

For the genome scan we selected 16 cases and 50 controls where the DNA was of sufficient quality. As before we carried out the analysis of this new dataset in two stages; the first compared 14 robust cases with 50 controls, and the second analysis added in the two less well-defined cases totalling 16 cases, again aligned to the same 50 controls. We subsequently combined these datasets with our previous 2013 study. In total we analysed up to 43 cases and 79 controls.

What were the results?

Unfortunately, from all of these analyses we were still unable to identify any regions of the DNA that are associated with epilepsy in the Keeshond. Therefore we are still unable to confirm the mode of inheritance of this condition in this breed. It could be that there are multiple recessive mutations, dominant mutation(s), or that the disease is genetically complex with several regions of the genome involved, perhaps with the involvement of environmental factors. We did have cases submitted to us that did not fit the typical pattern and age of onset of seizures, which might suggest that there is more than one type of epilepsy in this breed, although larger sample sets would be needed to confirm this.

What happens next?

To progress the study forward we need DNA from additional dogs. We suggest that we need a further 48 epilepsy cases and 48 older dogs that have never had a seizure, in order to conduct a new genome scan that we can add to our current data. Once we have these additional samples in place we can apply for funding for consumables to do this work.

What can we do to further this research?

As before, we continue to encourage submission of samples from Keeshonds with a robust diagnosis of idiopathic epilepsy and it helps us considerably if you can include as much

clinical information as possible with your submission. We also require samples from older Keeshonds, aged eight years or over, who have never had a seizure of any kind to act as controls in our study. We would be grateful for any health updates for dogs for which we currently hold DNA samples. For further information on how to submit a sample, or to send us updated health information, please email Bryan McLaughlin at bryan.mclaughlin@aht.org.uk.

Acknowledgements

We would like to thank all Keeshond owners and breeders who have submitted samples and information from their dogs. We also thank Anji Marfleet and Jane Saunders for their valued assistance in collecting samples for the study.