Genetic studies among Finnish Lapphunds **August 26th, 2009**

Background information

Finnish Lapphunds participate to the Canine Genetics Research performed in University of Helsinki, Finland (www.koirangeenit.fi). Professor Hannes Lohi and his research group have collected DNA samples from Lapphunds and Lapponian herders since 2005. The aim is to study genetics of idiopathic epilepsy and hereditary cataract (HC) in these two breeds.

Epilepsy research was started with clinical examinations of the selected epileptic and healthy dogs. Clinical analysis of Finnish Lapphunds included neurological examination, blood chemistry, electroencephalography (EEG) and magnetic resonance imaging (MRI) measurements. Neurological examination was normal in all dogs. Also no pathological findings were found from blood chemistry. None of the studied dogs had changes on MRI examination while some epileptic dogs showed epileptic activity in interictal EEG measurements. These results indicate that the epilepsy among Finnish Lapphunds is idiopathic.

Epilepsy afflicts over 1% of humans worldwide and represents a significant burden for our societies. Common epilepsy genes have proven difficult to track down in humans. Epilepsy is 5-10 times common in dogs and often fully recapitulates the human epilepsies. New genes discovered in dogs will be tested in respective human patient cohorts and eventually this will improve the health of both species. The epilepsy study among Lapphunds is part of the EU funded LUPA project (http://www.eurolupa.org/).

Another research project among Finnish Lapphunds and Lapponian Herders is hereditary cataract study. Cataract is an eye disease where opasifications form in the lens. These opasifications can be in different parts of the lens. Depending on the location cataract may have an effect to the dog's vision. In some cases the vision is completely lost. In both breeds multiple forms of hereditary cataracts are diagnosed. The main cataract in both breeds being posterior polar cataract (PPC). In PPC the opasicifications form in the back of the lens. Also cortical and punctuate cataracts are diagnosed. In Finnish Lapphunds the mean diagnosis age of the posterior polar cataract is 4 years and in Lapponian Herders mean is 4.5 years.

In humans cataract is the most common blindness causing eye disease and responsible for about 48% of world blindness. Gene discoveries in cataract will also be tested in human patient cohorts.

Current situation

A large pedigree showing all known epilepsy and HC cases has been constructed for both Finnish Lapphunds and Lapponian Herders. Pedigree analysis suggests complex, polygenic inheritance for both diseases.

We have tried to map both the epilepsy and hereditary cataract genes with genome wide association study. We picked epilepsy and HC cases from our DNA bank and selected healthy control to each affected dog. The best control dog is old (>7 years of age) and related to affected dog. In epilepsy study the control dog shows no

symptoms of epilepsy and in HC study the control dog must be eye examined and proven healthy at older age.

Unfortunately we got no clear association to any of the chromosomes by comparing epilepsy cases to healthy controls or by comparing HC cases to healthy controls. This implies that the genetics behind these two diseases is complex and the current sample numbers are too low to be able to identify the predisposing genes behind epilepsy and HC. Therefore we continue to collect additional samples from both affected and healthy dogs. In addition to blood sample we collect copies of the eye examination certificates from each eye examined dog. Furthermore, we wish that the owners of the epileptic dogs fill out an epilepsy questionnaire and return it together with the blood sample.

Blood sample submission instructions

Each owner must fill out the sample form and return it together with the blood sample. The form can be found from www.koirangeenit.fi (select in English from the left menu) or it can be ordered by email (eija.seppala@helsinki.fi or minna.s.virta@helsinki.fi).

1. Fill out the sample form for each sample and send it with your samples to our laboratory.

2. Include a copy of the dog's pedigree to the sample submission. If your dog has been eye examined, please send copies of the certificates together with the samples. If your dog is epileptic, please fill out the epilepsy questionnaire that can be found from the web page or ordered by email.

3. Collect 3-5 ml of blood to EDTA-tube.

4. Label the tube with the following information: Dog's registration name or registration number. Make sure that the same information is written to the sample form.

5. Invert the tube (8-10) times to prevent clotting.

6. Ship to the address at the end of the sample form. Please let us know to expect your sample by email in advance (eija.seppala@helsinki.fi or minna.s.virta@helsinki.fi)

7. Two to three day delivery services are the best. However, schedule the shipment so that it will NOT arrive during a weekend or holiday period. If the samples were collected at the end of the week, please store them in refrigerator (do not freeze) over weekend.

All information regarding the dog and the owner will be kept confidential and stored in a secured database. We select cases and controls from our DNA bank for future studies. If your dog's sample is used in research phase that leads to gene discovery, you will get the result of the gene test for free. After the gene and the mutation have been discovered, a commercial gene test will be offered for the rest of the dogs. The samples already sent to us can be used in testing and there is no need for additional

sample at the test phase. The same samples can be used in different studies, for example both in epilepsy and HC studies.

It is also very important that the dog owners update the health information of their dog if there are any changes after the sample has been sent to research laboratory.

Please remember that no genes have been discovered yet and the research can take time. But hopefully we are eventually able to offer gene tests for both epilepsy and hereditary cataract.

Best regards,

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