RESEARCH PROGRESS REPORT SUMMARY

Grant 01828: Mapping of Genetic Risk Factors for Canine Hip Dysplasia

Principal Investigator: Dr. Antti Iivanainen, DVM, PhD

Research Institution: University of Helsinki and the Folkhälsan Institute of Genetics

Grant Amount: $79,488.00

Start Date: 1/1/2014 **End Date:** 12/31/2016

Progress Report: Final

Report Due: 12/31/2016 **Report Received:** 12/31/2016

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Original Project Description:

Canine hip dysplasia is a common developmental disorder of the hip joint that severely affects a dog's quality of life. As the disease has several genetic risk elements and is influenced by environmental factors like diet and exercise, it is of paramount importance that genetic association studies are conducted using adequately-sized cohorts of genotyped diseased and healthy animals. Dr. Iivanainen will sample a large population of dogs (>300-400 dogs) so that contributing genetic loci can reliably be discovered. This research group expects that with such a strongly powered study all major genetic risk factors can be uncovered with a high statistical significance. Investigators expect that identified loci will be discovered across breeds. The identification of genetic risk elements will allow the development of genetic tests that can be used in breeding programs to control the disease incidence, as well as further studies regarding the possible role of diet and exercise in hip dysplasia development.

Grant Objectives:

1. To establish an accurately phenotyped primary study cohort for genetic studies. We aim to sample at least 300 cases and 300 controls.
2. To perform a GWAS for 144 cases and 144 controls using canine high density SNP arrays.
3. To replicate the associated loci in independent multinational cohorts of dogs in different breeds.

Publications:

In preparation.

Report to Grant Sponsor from Investigator:

The overall objective of our study is to perform a genome wide association study (GWAS) of canine hip dysplasia (CHD) in German Shepherds using a large sample cohort (200 cases and 200 controls). CHD is a common problem in many breeds. The dysplasia phenotype is graded from radiographs. In this study, we use the standards of Fédération Cynologique Internationale (FCI) ranging from A (healthy) to E (severely dysplastic). Each hip joint is graded individually. As the disease progresses also the risk for hip joint arthrosis – a painful and incurable condition – increases. The identification of genetic risk factors would enable the development of genetic tests to aid the breeders in controlling the disease. Four hundred animals consisting of carefully matched pairs of healthy and affected individuals should provide enough power for the association study to uncover the major genetic risk factors for this degenerative disease.

We have collected a large single-breed study cohort of 1141 German Shepherds including 411 cases and matched controls plus additional 319 controls. We have analyzed the association of CHD to a genome wide array of genetic markers using a subset of these dogs (N=497). The study revealed ca. 30 markers on eight different chromosomes that suggestively associated with the disease. Targeted replication studies using independent cohorts of dogs (German Shepherds N=244 and 11 breeds N=1767) have validated the findings from 3 chromosomes.

We are currently preparing several manuscripts based on our findings. The preliminary results were presented in the European Human Genetics Conference in Barcelona, Spain, on May 2016.