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: End-Year 2

Report Due: 12/31/2015 **Report Received:** 12/31/2015

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

Canine hip dysplasia (HD) is common a developmental disorder of the hip joint affecting many breeds and severely suppressing the quality of life. As the disease has several genetic risk elements and is additionally influenced by environmental factors like feed and exercise, it is of paramount importance that the genetic association studies are conducted using adequately-sized cohorts of genotyped diseased and healthy animals. This proposal involves two research groups (Finland and France) engaged in the genetics of HD in German Shepherd, Golden retriever and Labrador retriever breeds. HD is a polygenic disease and requires large enough sample sizes (>300-400 dogs) so that contributing genetic loci can reliably discovered. This proposal aims to genotype 288 dogs in German Shepherds increasing the total number of studied dogs in this breed over 400. By doing this, we expect to increase the power of the association studies so that all major genetic risk factors can be uncovered with a high statistical significance. The loci identified in German Shepherds will be followed up in the other breeds. The identification of genetic risk elements allows developing genetic tests that can be used in breeding programs to control the disease incidence as well as further studies regarding the possible role diet and exercise in the HD 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:

None at this time.

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.

At present, we have collected a study cohort of 1141 dogs including 411 cases and 730 controls. From the study cohort, we have thus far genotyped 167 severe (“D” or “E” hip joints) and 38 mild (“C” or “D” hip joints) cases and matched controls (“A” hip joints) for all of them (see the figure below).

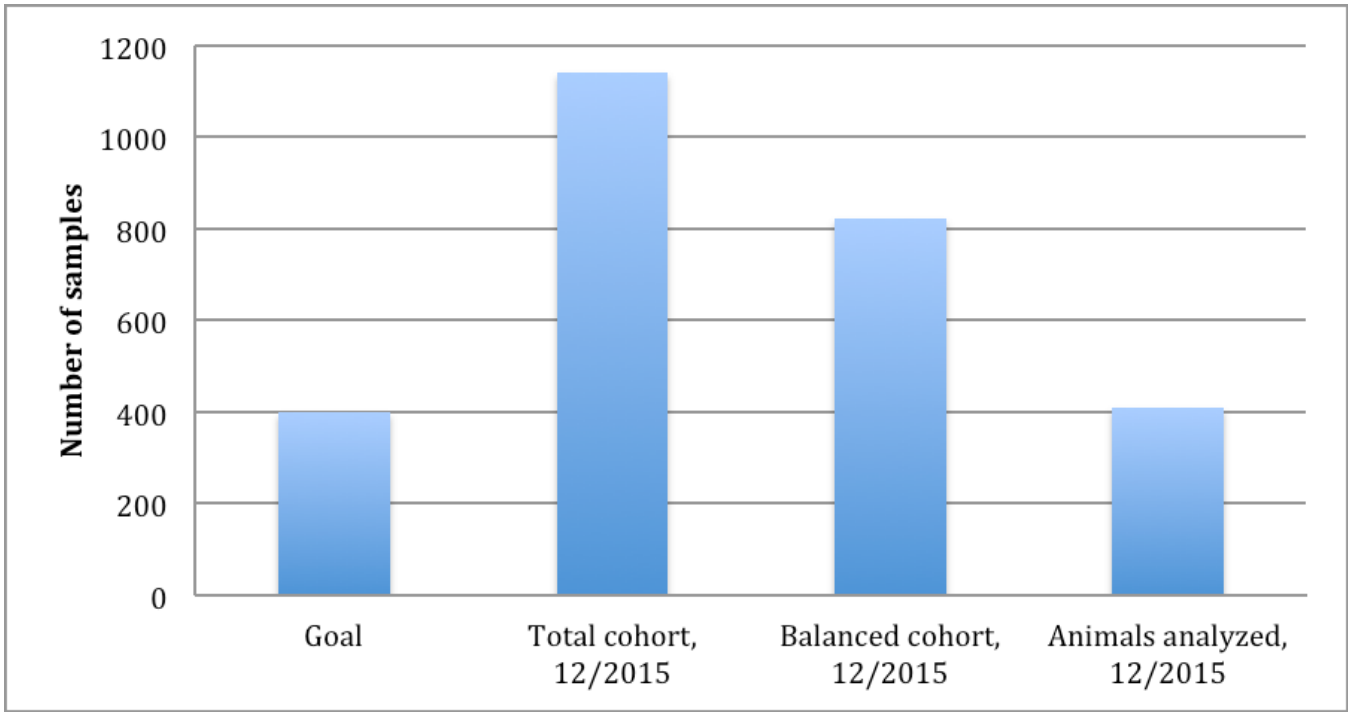

Figure. The present size of the total sample cohort (with C-, D-, or E-graded cases and A-graded controls), balanced cohort (with C-, D- or E-graded cases and individually matched A-graded controls), and the number of determined genotypes from the balanced cohort in relation to the overall objective of genome-wide association study using 200 dysplastic and 200 control dogs.

Since last report in June 2015, we have collected an independent second cohort (833 dogs, four breeds) and performed larger genome-wide association study with 526 dogs. Several clusters of SNPs suggestive of association were detected in eight chromosomes. The validation of these SNPs will take place in 2016 using the independent second cohort.