



AMERICAN KENNEL CLUB
**CANINE HEALTH
FOUNDATION**
PREVENT TREAT & CURE

GRANT PROGRESS REPORT REVIEW

Grant: 01268: *Investigation to identify genes associated with canine immune-mediated haemolytic anaemia*

Principal Investigator: Dr. Lorna J. Kennedy, PhD

Research Institution: University of Manchester

Grant Amount: \$68,339.56

Start Date: 1/1/2010 **End Date:** 6/30/2011

Progress Report: 12 month

Report Due: 12/31/2010 **Report Received:** 12/21/2010

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:

Background: Immune-mediated haemolytic anaemia (IMHA) is the most common immune-mediated disease of the dog, representing a major health concern to this species. There are several breeds that are predisposed to developing IMHA, including the Cocker Spaniel, the English Springer Spaniel and the Clumber Spaniel. The researchers have previously identified an association of IMHA with some immune function genes, and have also performed a genome wide search for other genes involved in the disease. This has identified several other regions of the genome that are statistically associated with IMHA.

Objective: The researchers aim to confirm these findings, investigate these areas further, and identify other potential susceptibility genes. The identification of one or several genes associated with IMHA could be used to develop a screening test that could indicate the risk of an individual dog developing IMHA. This would be of great importance to owners and breeders of dog breeds that are susceptible to this devastating disease.

Grant Objectives:

Objective 1: To perform a more in-depth analysis of existing GWAS data, including further meta- analyses and permutation testing

Objective 2: To perform replication studies in a large cohort of cases and controls, to confirm genetic associations previously identified by GWAS, in Cocker and Springer Spaniels affected with Immune-Mediated Haemolytic Anaemia (IMHA)

Objective 3: Identify SNPs using long range DNA sequencing of the two most significant confirmed regions of association, that are shared across both breeds

Objective 4: To refine and localize these areas of association.

Publications:

Report to Grant Sponsor from Investigator:

Previously the AKC gave us some funding for a pilot study on immune-mediated haemolytic anaemia (IMHA). This involved doing a whole genome scan comparing healthy cocker and springer spaniels with affected dogs, in order to identify regions of the genome that might be associated with IMHA. A preliminary analysis revealed several potential regions of interest.

We have now performed a replication study testing those regions for associations using a larger group of over 300 dogs. Disappointingly, none of the markers were confirmed in the replication study as having an association with IMHA.

We have obtained extra data for control dogs of both breeds and reanalysed the original data, hoping that this increased power would reveal some stronger associations. New analysis methods are being developed all the time, and there is, as yet, no standard method for such analyses. We have contacted many collaborators, and are testing out various different approaches.

We cannot proceed with fine mapping based on these results, as there is no strong evidence for one region of the genome to investigate. We therefore propose to test some extra cases on the high density array, to increase the power of the experiment.

We are also part of a large European study (known as the LUPA project) investigating canine diseases. We have seen many of the early studies within LUPA starting with low sample numbers on low density arrays and unable to identify associated markers, which have gone on to test additional cases on the high density array, and then found some strong associations.