RESEARCH PROGRESS REPORT SUMMARY

Grant 02257: Identification of Genetic Risk Factors for Canine Epilepsy

Principal Investigator:  Dr. Gary S. Johnson, DVM PhD
Research Institution:  University of Missouri, Columbia
Grant Amount:  $84,121.00
Start Date:  5/1/2016   End Date:  4/30/2017
Progress Report:  Mid-Year 1
Report Due:  10/31/2016   Report Received:  11/1/2016

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:

Epilepsy is one of the most common neurologic diseases of dogs and a top concern of dog breeders. In spite of strong evidence that genetics is important in determining the risk of the common idiopathic epilepsy, numerous gene mapping studies have failed to identify a locus that accounts for that risk in either dogs or humans. Seizures occur when excessive activity goes beyond the normal threshold for brain function and many factors contribute to that level of activity. Thus it is thought that mutations in numerous genes can collectively contribute to increased activity until that threshold is exceeded, resulting in epilepsy. Any one of these mutations may be present in non-epileptic dogs as well, but because it only partially alters activity it would not produce seizures. This would, however, cause traditional gene mapping studies to overlook that mutation. Using a novel whole genome sequencing approach we will identify DNA variations in epileptic dogs that could affect the function of genes such as ion channels and neurotransmitter receptors that have been shown to alter the seizure threshold in humans or rodents. We will then directly compare the frequency of those variations in populations of epileptic and non-epileptic dogs rather than using the indirect markers used in traditional mapping studies. We predict that the increased power provided by looking for specific candidate variations rather than linked markers will permit the identification of epilepsy risk factors. These can then be developed into DNA tests to enable breeders to select against those risk factors.
Publications:

In preparation.

Report to Grant Sponsor from Investigator:

We proposed to generated and analyze whole genome sequences from 10 epileptic dogs. So far we have used AKC CHF funds to generate whole genome sequences for 8 epileptic dogs and we have analyzed 5 of these whole genome sequences. By the end of 2016, we expect to have generated and analyzed all 10 of the whole genome sequences. In addition, we have used funds from other sources to generate and analyze whole genome sequences for 4 additional epileptic dogs and 3 more epileptic dogs are scheduled for sequencing and analysis before the end of 2016. Once the whole genome sequences of all 17 epileptic dogs have been generated and analyzed, we will select 7 or more of the most promising epilepsy risk factor candidate mutations from these whole genome sequences and determine whether or not they occur more frequently in epileptic dogs than in epilepsy-free dogs of the same breed.

We have also proposed to select 15 to 25 of the most promising epilepsy risk factor candidate mutations from approximately 500 canine whole genome sequences and determine whether or not they occur more frequently in epileptic dogs than in epilepsy-free dogs without regard to breed. This portion of the research is behind schedule because of unforeseen delays in the reconfiguration of a University supercomputer. The problem now appears to be rectified and we have asked for a 6-month no-cost extension of the funding period to allow us to complete this aspect of the proposed research.