RESEARCH PROGRESS REPORT SUMMARY

Grant 02242: Understanding the Genetics of Adverse Drug Reactions in Sighthounds

Principal Investigator: Dr. Michael H. Court, BVSc, PhD

Research Institution: Washington State University

Grant Amount: $150,000.00

Start Date: 2/1/2016 **End Date:** 1/31/2018

Progress Report: Mid-Year 1

Report Due: 7/31/2016 **Report Received:** 10/21/2016

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Original Project Description:

Life-threatening unanticipated reactions to drugs with a narrow margin of safety (such as those used for anesthesia and to treat cancer) are a common concern for dog owners and veterinarians. However, research conducted at Washington State University has enabled development of a simple cheek swab test (the MDR1 gene test) that is now being used by veterinarians to identify dogs that should either avoid or have reduced doses of certain drugs used to treat cancer and parasite infections. Using a similar strategy the investigators have been conducting research to identify the cause of extremely slow recovery from anesthesia (up to several days) in a high proportion of greyhounds, and also in other sighthound breed dogs (such as Scottish deerhound, Borzoi, Whippets, etc.). The investigators have recently discovered a mutation in a gene that is known to be essential for metabolism (breaking down) many commonly used anesthetic drugs (such as propofol), as well as many other drugs used in dogs. Interestingly in addition to sighthound breeds, this gene mutation is also found in some other breeds such as Border Collies. The purpose of this research project is to prove that this mutation can cause decreased drug metabolism, while also determining which drugs and which dog breeds are likely to be most impacted. The ultimate goal of this study is to develop a genetic test that could be used by veterinarians to guide the safe use of these drugs in dogs with the gene mutation.

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

The first 6 months of this grant have been spent laying the groundwork for what we hope to be a very productive next year of research. Dr. Stephanie E. Martinez, PhD was hired as the postdoctoral researcher for this project and began on April 1, 2016. Since her hire, we have identified a system using insect viruses and insect cells that allows us to make the dog enzyme involved in breaking down drugs, including anesthetics. We had the enzyme's DNA sequence made - with and without the newly discovered mutations - and we successfully put those DNA sequences into insect viruses. We then infected insect cells with these viruses. These insect viruses take over the insect cell's protein synthesis factory to make our dog enzymes. We have been collecting these enzymes by breaking open the insect cells and we're currently working to optimize how much virus to infect the insect cells with to maximize the amount of enzyme made. After we figure out the precise amount of virus to add to the insect cells as well as how long to let the infection go on for before we collect the enzymes, we will begin comparing the activity differences of the regular enzyme with the mutated versions of the enzyme along with how much of the mutated enzymes are made in comparison to the regular enzyme.