Research Progress Report Summary -- Grant 02165-MOU

Grant 02165-MOU: Identification of Biomarkers and Therapeutic Targets for Canine Degenerative Myelopathy: The Search for A Cure

Principal Investigator: Dr. Joan R. Coates, DVM

Research Institution: University of Missouri, Columbia

Grant Amount: $154,077.00

Start Date: 1/1/2015 **End Date:** 12/31/2016

Progress Report: End-Year 1

Report Due: 12/31/2015 **Report Received:** 12/28/2015

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:
Degenerative myelopathy (DM) is an adult onset disease of the spinal cord causing progressive weakness and paralysis of the hindlimbs and eventually all limbs. Mutations in an enzyme that converts superoxide to water and hydrogen peroxide, superoxide dismutase 1 (SOD1), have been linked to DM and amyotrophic lateral sclerosis (ALS-Lou Gehrig's disease). DM is associated with degenerative loss of axons, which transmit signals from the brain and spinal cord to their targets (muscle). Currently no diagnostic test exists that would allow for repeated measurements with minimal invasiveness. We are proposing to develop a test that would assay the blood and cerebrospinal fluid (CSF) for proteins that are exclusively found in axons under non-disease conditions, referred to as neurofilament proteins. We will correlate the concentrations of neurofilament proteins in CSF and blood with disease stage, and we anticipate that neurofilament protein concentration in blood and CSF will increase as disease progresses. Such a test will allow for minimally invasive monitoring of disease. Furthermore, such a diagnostic test could be used to measure the success of therapy, which may be underway in a cohort of DM-affected dogs [Boxers and Pembroke Welsh Corgis (PWC)] (funded by NIH/NINDS). We will complement the test for neurofilament proteins with other studies that measure disease progression such as specific MRI techniques to evaluate the brain and spinal cord and electrical testing of the muscle and nerves. These are functional disease markers that are also being studied in ALS patients.

Grant Objectives:
1) To establish that neurofilament proteins can be detected in the blood and cerebrospinal fluid of degenerative myelopathy (DM) affected dogs.
2) To demonstrate that neurofilament protein concentrations in blood and cerebrospinal fluid is a valuable biological marker for assessing clinical progression in degenerative myelopathy dogs.

Publications:
Manuscript in preparation.

Report to Grant Sponsor from Investigator:
Degenerative myelopathy (DM) is an adult onset disease of the spinal cord causing progressive weakness and paralysis of the hindlimbs and eventually all limbs. Mutations in an enzyme that protects the spinal cord from oxidative stress have been linked to DM and amyotrophic lateral sclerosis (ALS-Lou Gehrig's disease). DM is associated with degenerative loss of axons, which transmit signals from the brain and spinal cord to their targets (muscle). Monitoring the progression of disease is critical for development of effective therapies, but currently no diagnostic test exists that would allow for repeated measurements with minimal invasiveness. We have developed a test that would assay the blood and cerebrospinal fluid (CSF) for proteins that are exclusively found in axons under non-disease conditions, referred to as neurofilament proteins. We are in the process of correlating the concentrations of neurofilament proteins in CSF and blood with disease stage. Preliminary data suggests that measuring neurofilament proteins in CSF is a diagnostic marker for DM. We have shown that pNF-H in CSF remains elevated through all 4 disease stages. We will measure neurofilament proteins in CSF and serum to measure the success of therapy in a cohort of DM-affected dogs (funded by NIH/NINDS). We will complement the test for neurofilament proteins with other studies that measure disease progression such as specific MRI techniques to evaluate the brain and spinal cord and electrical testing of the muscle and nerves. These are functional disease markers that are also being studied in ALS patients. After additional safety testing, commencement of the therapy study is underway.