Public Abstract

First Name:Kara

Middle Name:Ann

Last Name:Osterbur

Adviser's First Name:Amy

Adviser's Last Name:DeClue

Co-Adviser's First Name:

Co-Adviser's Last Name:

Graduation Term:SS 2012

Department:Veterinary Medicine and Surgery

Degree:MS

Title:THE MECHANISM OF C-TYPE NATRIURETIC PEPTIDE PRODUCTION IN DOGS AND ITS USE AS A PROGNOSTIC INDICATOR IN CRITICALLY ILL DOGS

Sepsis in canine populations is a serious problem and is associated with substantial morbidity and mortality. Rapid identification of sepsis is crucial to providing proper treatment in a timely fashion and biological markers, or biomarkers, can aid in the diagnosis of sepsis. A circulating protein in the body known as the N-terminal portion of pro C-type natriuretic peptide (NT-pCNP) has shown promise as a diagnostic biomarker for sepsis in humans and dogs. Dogs with sepsis have significantly greater concentrations of NT-pCNP compared to healthy dogs and dogs with other forms of critical illness. The mechanism of NT-pCNP induction in dogs is unknown and this information is key to guide further research using NT-pCNP as a biomarker. In addition to diagnostic biomarkers, there is a need for prognostic biomarkers to allow clinicians and pet owners to make more informed decisions regarding treatment and for proper stratification in clinical trials. NT-pCNP has not been extensively evaluated as a prognostic biomarker for canine sepsis.

In order to determine the mechanism of NT-pCNP induction, a canine aortic endothelial cell culture model was used. The cells were stimulated with various concentrations of bacterial products and inflammatory mediators and discovered that NT-pCNP concentrations were significantly higher when the cells were stimulated with lipopolysaccharide (a bacterial product), tumor necrosis factor-alpha and interleukin-1 beta (inflammatory mediators), which are all known to be important in the pathogenesis of sepsis. These results were both time and dose dependent in nature. This experiment provides insight to why dogs with sepsis have greater concentrations of NT-pCNP compared to dogs with other forms of critical illness.

In order to determine if NT-pCNP can be used as a prognostic indicator for critically ill dogs, a prospective observational study was performed in order to discover if NT-pCNP concentrations at admission are significantly different in dogs who survive compared to dogs that do not. The initial serum NT-pCNP concentrations of all critically ill dogs over 6 months old that were admitted to the intensive care unit were determined and dogs with a positive NT-pCNP concentration were included in the study. Serial samples in a smaller number of dogs were also evaluated to determine if serial NT-pCNP concentrations are useful for predicting prognosis. However, serial NT-pCNP concentrations and NT-pCNP concentrations at admission were not useful in predicting outcome and should therefore not be used as a prognostic biomarker.

This research has provided information on NT-pCNP induction in dogs and has opened the door to future research examining NT-pCNP induction from other canine cell types. Additionally, this research has determined that NT-pCNP is not a useful prognostic biomarker for critically ill dogs and more research is now needed to determine the optimal prognostic biomarker.