I. Title and Abstract

Title: Histologic and biomechanical characterization of clinical equine tendon disease and subsequent *in-vitro* model development for assessment of current therapies.

Subject: This project will increase our understanding of tendon disease and foster the development of a laboratory model of tendonitis in which novel treatments may be evaluated. The target population is all athletic horses who may suffer from tendonitis, given the reported incidence rate of 37% across all disciplines.

Significance: This project is being done because tendonitis is a leading cause of equine injury, and novel therapeutics are needed to increase the rate at which injured horses recover from tendonitis as well as improve the re-injury rate. Superficial digital flexor tendons (SDFT) once damaged heal slowly, with as few as 20% of injured horses successfully returning to work. Yet up to 67% will suffer a re-injury within 2 years, even given the current therapeutic practices. While new therapeutics for tendonitis are needed, their development is hindered as the histologic, biomechanical, biochemical, and cellular properties of clinical disease are poorly understood. Furthermore, even less is known about the associations among these properties. Therefore, the significance of this project is to establish a laboratory platform on which therapeutics may be studied by: 1) characterizing disease-associated properties across the range of damage seen in clinical tendon disease, and 2) developing an *in-vitro* model which emulates natural tendonitis. This project is relevant to the MAF because it addresses a large problem in equine medicine by posing a solution that does not require the sacrifice of horses.

Hypothesis/Objectives:

Hypothesis: Histologic changes in equine tendonitis are significantly associated with changes in tendon MR images, biomechanical function, extracellular matrix, biochemical composition and gene expression.

Aim 1: Using fresh post-mortem tendons possessing a range of clinical tendonitis, the existence of a significant association between histological, MR images, biomechanical function, extracellular matrix, biochemical composition and gene expression will be assessed using multivariate analysis.

Objective 1: Using fresh post-mortem tissue from normal tendon, the separate or combined use of strain overload, focal disruption, or chemical degradation will allow the feasible recreation of *in-vitro* tendonitis as characterized in Aim 1.

Future Aim: The *in-vitro* tendon disease model developed in Objective 1 will be used to study current therapies in regenerative medicine.

Study Design: SDFT will be collected from a group of athletic horses that will be euthanized for reasons unrelated to this project, which will provide a range of clinical tendonitis samples. Aim 1 will provide characterization of clinical tendonitis using an array of outcome parameters. These outcome parameters will be used to guide the creation of an *in vitro* model of tendonitis using healthy tendon.

Timeline: Tendon samples from clinical cases will be collected over the course of the first year. Year 2 will be used for model development and evaluation.

Expected Results: Based on our collaborator experience from Racehorse Associations, findings will include a wide range of clinical tendonitis for study in Year 1. Analysis as outlined in Aim 1 should result in characterization of clinical tendonitis, and through mechanical overload, focal disruption, and/or chemical degradation, a laboratory model that replicates clinical disease will be constructed.

Anticipated Outcomes: This study will significantly increase our understanding of clinical tendon disease in horses and will produce a useful laboratory model for the study of current and novel disease therapies.

Potential Impact for Animal Health: This study will provide a better understanding of clinical tendonitis in the horse and the means to test current and novel therapeutics *in vitro* without animal usage. Ultimately, this will lead to the development of improved tendon healing techniques that lower re-injury rates for all inflicted horses.