



RESEARCH PROGRESS REPORT SUMMARY

Grant 01844: Treatment of Urinary Incontinence with Multipotent Muscle Cells: A Regenerative Medicine Approach to a Common Canine Health Problem

Principal Investigator: Dr. Shelly Vaden, DVM, PhD

Research Institution: North Carolina State University

Grant Amount: \$116,184.24

Start Date: 1/1/2013

End Date: 12/31/2016

Progress Report: Mid-Year 4

Report Due: 6/30/2016

Report Received: 7/29/2016

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:

Urinary incontinence affects more than 20% of spayed female dogs, with medium and large breeds more commonly affected. In the majority of the cases urinary incontinence is caused by dysfunction of the muscles controlling the urethral sphincter. This results in uncontrolled loss of urine and can lead to serious bladder and kidney infections, in addition to irritation and/or ulceration of the skin in contact with the urine. Treatment can include hormone therapy, drugs designed to strengthen the muscle tone of the urethral sphincter, collagen injections, or surgery. Recently, we have reported that injection of muscle progenitor cells into damaged urethral sphincters can restore normal function in dogs. The purpose of this project is to extend those observations and examine the usefulness of cultured muscle cells for the restoration of function of the urethral sphincter in dogs with naturally occurring urinary incontinence. Briefly, a small muscle biopsy will be obtained from the affected dog, and muscle progenitor cells isolated and grown in culture. After expansion, the cells will be injected into the urethral muscularis and the dogs allowed to recover. The effects of the procedure will be determined by owner reported continence scoring and urodynamic measurements and the animals will be followed for a period of 24 months to determine the long term effects on the procedure.



Publications:

Williams K, The Future Of Veterinary Stem Cell Therapies. ITERA-FAT-STEM Meeting. 2015.

Vaden SL, Mathews K, Williams K, Reynolds H, Gleason K, Harris T, Manning K, Piedrahita J. Regenerative medicine approach to the treatment of urinary incontinence in female dogs. ACVIM Forum 2016. Abstract. J Vet Intern Med, 2016, 30:1541.

Report to Grant Sponsor from Investigator:

Aim 1. Effect of aging on isolation and expansion of muscle progenitor cells (MPCs).

Muscle biopsy specimens have been collected from eight dogs of different ages and different body condition scores immediately following euthanasia for a variety of causes. Muscle progenitor cells (MPCs, also known as 'satellite cells') needed for the proposed injections are separated from the mature muscle cells. The MPCs are subsequently grown under sterile culture conditions and the time required to generate 100 million cells has been recorded depending on the age, body condition score, or muscle that the biopsy was collected from (trapezius, triceps, or semimembranous muscle).

Based off of the data collected so far, the required number of cells can be generated regardless of the age or muscle biopsied; however, dogs with a higher body condition score (i.e. higher percentage body fat) appear to take longer to generate the same number of cells. Once we have clinical efficacy outcome data from patients in the clinical trial, we will be able to further evaluate the effects of these different factors on muscle progenitor cell growth patterns. In addition to these factors, we will also be evaluating a variety of muscle cell markers via qPCR and immunofluorescence and comparing these markers to the ultimate clinical outcome of the patients to determine whether we can predict clinical outcome based off of the initial quality of the biopsy specimen.

Aim 2. Effect of surgical versus endoscopy-guided MPC injection for long-term correction of USMI.

To date, 11 patients have been enrolled and treated; 2 more are scheduled for enrollment. All dogs had urinary incontinence at rest from between 8 months and 5 years duration that was not responsive to standard medical management. Most of these dogs have had a good response. Only one did not have any response at all. None of the patients had any complications following the injection.