



RESEARCH PROGRESS REPORT SUMMARY

Grant 02263-MOU: Characterization of Kidney Disease in Dalmatians

Principal Investigator: Dr. Rachel E Cianciolo, VMD, PhD

Research Institution: Ohio State University

Grant Amount: \$31,434.00

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Progress Report: Mid-Year 1

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(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:

Chronic kidney disease is a significant progressive problem in dogs. Some breeds (e.g. Dalmatians) are predisposed to developing kidney disease. Two different hereditary diseases of the urinary system have been reported in Dalmatians: urinary stone formation (urolithiasis) and a defect in the glomerulus, which is the filter of the kidney. These two diseases cause distinct clinical signs: urolithiasis leads to urinary tract obstruction while glomerular disease results in protein loss into the urine (proteinuria). The genetic cause of urolithiasis is known while the genetic cause of glomerular disease has not yet been identified. Although one specific type of glomerular disease has been reported in the literature, our preliminary investigations indicate that there are multiple causes of proteinuria in Dalmatians. Evaluation of kidney tissue by the International Veterinary Renal Pathology Service has revealed many diverse types of glomerular diseases in Dalmatians, at least 4 of which might be hereditary. Therefore, the most common disease type is unknown and must first be identified. Here, we propose a detailed review of autopsy and biopsy sample archives that have been previously obtained from Dalmatians with proteinuria. Next, prospective examination of select kidney samples with advanced techniques (electron microscopy and immunofluorescence) will ensure the accurate diagnosis of the glomerular disease. Genetic analysis can then be performed on related dogs that demonstrate similar glomerular lesions. These analyses will include sequencing the genome of dogs so that candidate genes previously associated with glomerular disease can be examined to identify possible mutations.



Publications:

None at this time.

Report to Grant Sponsor from Investigator:

The primary goal for this project is to identify and characterize a type of kidney disease in Dalmatians, which might be hereditary. A popular sire was used a few years ago and died with proteinuria, which indicates that he had a type of kidney disease that caused him to lose large amounts of protein in his urine. Since then, many of his progeny have had similar symptoms. Thus there is concern among Dalmatian breeders that this proteinuric kidney disease might have a genetic basis.

There has been one previous publication that documented a certain type of hereditary proteinuric kidney disease (known as canine Alports syndrome) in a lineage of Dalmatians in Australia. However, it was unclear whether or not American Dalmatians had the same type of disease. In fact, none of the Dalmatian kidney samples previously submitted to the International Veterinary Renal Pathology Service (IVRPS) had lesions consistent with canine Alports syndrome. Therefore, the first step for this project is to diagnose the type of changes that occur in kidneys of proteinuric Dalmatians. After characterizing the disease types, we can then evaluate the pedigrees to determine the best candidate genes (and/or dogs) for genetic testing. This will also help us determine which type of genetic analysis would be the most suitable.

Collection of kidney tissue, serum and urine are all routine steps in the diagnosis of proteinuric kidney disease. We plan to collect "archived" samples from Dalmatians that were autopsied or biopsied prior to the commencement of the study. We will re-analyze the glass slides of these samples with special stains. As of yet, we have re-examined 8 Dalmatian kidney samples that were archived at the Ohio State University since 2005. At Texas A&M University, 16 Dalmatians have been autopsied since 2005 and re-examination of those samples is ongoing. We have created a flyer to advertise this part of our study of archived tissue (and submitted pedigree) from any Dalmatian owner whose dog died with kidney disease. This re-examination of tissue will be at no cost to the owner.

We also need to examine prospectively collected kidney, urine, serum and whole blood from newly diagnosed Dalmatians. Although we encourage owners to allow kidney biopsies to be obtained from their proteinuric Dalmatians (so we can try to detect the early stages of disease), we accept autopsied kidney samples as well. We anticipate that submission of minimally invasive samples (blood and urine) will represent many more dogs/pedigrees than the kidney biopsies. Urine and blood samples can also be submitted from proteinuric Dalmatians that cannot be biopsied and from dogs related to those affected by kidney disease, whose owners would be willing to consent to sample collection. These samples will help us to create an



extensive pedigree of affected and unaffected Dalmatians. As mentioned previously, biopsied kidney tissue, urine and serum are all considered routine diagnostic samples, which will help guide therapy for the dog. However, whole blood for DNA isolation is not considered to be a sample used for diagnosis of kidney disease. We obtained approval from the IACUC at Texas A&M, where the whole blood will be processed to harvest DNA. Upon this approval, we created a flyer to distribute to Dalmatian breeders and owners, as well as all veterinarians that submit samples to the IVRPS. We have worked hand in hand with the Dalmatian Club of America Foundation (DCAF) to distribute the flyer and have already received inquiries about sample submission. To date, we have examined kidney tissue, urine and serum from one proteinuric Dalmatian as well as urine and serum from 2 additional Dalmatians. Once the study is in full swing, we anticipate many more samples to be submitted for evaluation, and our conversations with the DCAF have indicated that many breeders and owners have been discussing the logistics of submitting samples.

The last part of our study is dependent on the results from these first steps. If we identify a specific type of proteinuric kidney disease that demonstrates a pattern of inheritance, then we will select the best candidate dogs for genetic sequencing. This last step will be done in conjunction with analysis of the pedigree and the guidance of the geneticist for our study. This type of informed approach will ensure that we are examining DNA from Dalmatians that are affected by a similar disease process.