



RESEARCH PROGRESS REPORT SUMMARY

Grant 02507: Characterizing Developmental Lung Disease as a Cause of Sudden Death in the Norwich Terrier

Principal Investigator: Kurt Williams, DVM, PhD
Research Institution: Michigan State University
Grant Amount: \$116,076.00
Start Date: 3/1/2018 **End Date:** 2/28/2021
Progress Report: Mid-Year 2
Report Due: 8/31/2019 **Report Received:** 10/12/2019

(The content of this report is not confidential and may be used in communications with your organization.)

Original Project Description:

Neonatal respiratory distress syndrome has been attributed to more than 60% of deaths early in life in puppies. The underlying cause(s) of this apparently common problem is poorly understood. Despite the high frequency of respiratory-related mortality in neonatal puppies, there are no reports describing the underlying lung pathology in affected individuals. In human medicine the classification, management and evaluation of diffuse interstitial lung diseases in infants are well described. The most severe neonatal lung diseases in humans develop as a result of abnormal development of the lung, and often result in death soon after delivery. The investigators recently documented microscopic evidence of striking abnormal lung development in puppies of various breeds who died suddenly, suggesting that developmental lung disease (DLD) is an important and unrecognized cause of early death in young puppies. Breeders of Norwich Terriers (NT) report that sudden death of puppies early in life is common. Through preliminary studies, a high incidence of DLD in NT puppies associated with sudden death has been identified. The identification of a breed-association with DLD in the NT presents an opportunity to correlate the pathology and genetics to sudden death in NT puppies. Findings could lead to the development of preventive measures to reduce the incidence of DLD in the NT as well as other dog breeds, and may also be applicable to similar developmental lung diseases in children.

Publications: None at this time.



Presentations:

Brandon Franz was a DVM summer research student working on the 3D vascular reconstruction of DLD in the Norwich Terrier. Brandon presented his data at the National Veterinary Scholars Symposium. The title of his poster presentation was 'Evidence of Intrapulmonary Vascular Anastomoses in Developmental Lung Disease in the Norwich Terrier'.

Report to Grant Sponsor from Investigator:

We have made considerable early progress in advancing our understanding of developmental lung disease in the Norwich Terrier. Developmental lung disease (DLD) appears to be an important contributing factor in early life death in puppies of this breed of dog. We are using a 2-pronged approach to investigate this poorly understood disease: investigating intricacies of the structural abnormalities in lungs from affected puppies, and pursuing a genetic basis for this disease in the Norwich Terrier (NT). We used specialized computer software to take 2D images and structures in the lung and convert them into 3D images to investigate abnormalities in the lungs of affected puppies, especially abnormalities in blood vessels. Using this technique we have data that strongly suggests that there are abnormal pathways that allows a percentage of blood flow to bypass the normal pathway through the lungs.

The second major goal of our research is to look for a genetic basis for this disease in the NT. Our initial efforts to identify a genetic basis for this disease utilized genome wide sequence analysis (GWAS). These efforts did not identify an obvious genetic defect. This is not entirely unexpected. GWAS may miss complex genetic diseases. Because of this we are now going forward with sequencing the entire genome of related normal and affected Norwich Terriers. Thanks to the efforts of NT breeders, we have identified a litter which lost a puppy to DLD, but which also has normal siblings. This family of Norwich Terriers allows us a source of DNA for sequencing. At this time we have the samples from this family of NT dogs and are working to get the DNA samples properly prepared such that we can perform the sequencing of the entire genome. Sequencing the entire genome will result in a large amount of data to process. We are hopeful that analysis of this data will detect the genetic defects underlying this important cause of death in NT puppies.