

Buttons Fund for Feline Chronic Kidney Disease Research Annual Report 2021

The Buttons Fund for Feline Chronic Kidney Disease Research supports cutting-edge research in chronic kidney disease in cats as well as other feline-related research. Under the direction of Dr. Jessica Quimby, DVM, PhD, DACVIM (Internal Medicine), this research includes projects designed to understand the mechanisms of renal aging and disease, assess the efficacy of medications to improve the outcome and quality of life for chronic kidney disease cats, as well as investigations into novel treatment strategies, which are then tested via a rigorous clinical trials program.

Current Fund Vision

- One of the major aims of the fund is to support clinical studies for CKD cats, typically ranging from \$10,000-30,000 per study.
- Another major fund aim is to support veterinary students' involvement in feline research. For several years Buttons Fund has supported students to participate in the Summer Scholars Program (\$5000/student).
- A second educational aim is to support interns and internal medicine residents in their involvement in feline research. Currently three young doctors are participating in projects supported by Buttons Fund. Support of these research studies promotes interest in feline research and helps residents meet the requirements for their graduate program and the publication requirement for board certification in small animal internal medicine.
- We would also like to consider the future vision of continuing the feline research intern experiences, and attracting Master's and PhD student candidates.

Studies Supported By Buttons Fund in 2021

The following studies were completed in 2021:

- *Expression of CD31 in feline kidneys to characterize peritubular capillary density in CKD*
 - Feline CKD is characterized by tubulointerstitial inflammation, tubular loss and fibrosis. Hypoxia is a key driver of fibrosis and its pathophysiology is associated with capillary rarefaction (reduction in vascular density) in humans. The goal of this study was to determine if similar vascular changes occur in cats with CKD. This study found that some cats with CKD did have very small percentage of capillary area remaining in their kidney.
 - Abstract: Paschall R, Quimby JM, Cianciolo RE, Mcleland SM, Lunn KF, Elliott J. Assessment of capillary rarefaction in cats with and without CKD. Presented at American College of Veterinary Internal Medicine Forum 2021. Poster Presentation. This paper will be submitted for publication by the end of November.
 - Dr. Rene Paschall participated in the Summer Scholars program as a veterinary student supported by Buttons Fund in 2018 to initiate this project. Dr. Paschall has completed

Dr. Quimby's research internship, and is currently a rotating intern. She has been accepted as an internal medicine resident for next year based on her progress!

- *Validation of Ghrelin Sample Storage and Stability in Healthy Cats*
 - Ghrelin is often called the “hunger hormone”. Unfortunately, ghrelin requires very particular handling and storage to maintain its chemical structure. The purpose of this study is to assess differences in blood sample storage protocols and whether prolonged storage affects the concentration of this hormone within blood samples. This study is to prepare to evaluate differences in appetite regulation between healthy cats and those with chronic kidney disease. It was found that acidifying the samples does increase their stability during storage. Excitingly this pilot data allowed us to successfully apply for a grant from EveryCat Health Foundation (W21-042 Hormonal regulation of appetite in cats with and without CKD) to further this work!
 - Abstract: Lorbach SK, Quimby JM, Brusach KK, Kinsella H, Toribio R. Ghrelin sample storage and stability in healthy cats. Presented at American College of Veterinary Internal Medicine Forum 2021. Poster Presentation. This paper will be submitted for publication by the end of December.
 - Dr. Sarah Lorbach is an internal medicine resident/Master's degree student who was Dr. Quimby's research intern prior to starting her residency. This project comprises part of her Master's Thesis.

- *Histologic assessment of the aging feline kidney in cats without kidney disease.*
 - In humans, histopathologic changes occur in the kidney even before clinical kidney disease is evident. The goal of this study was to describe the pathology present in the kidneys of cats over a wide age range who had no clinical indication of CKD. It was found that similar to humans, renal aging in cats without CKD is characterized by increasing glomerulosclerosis, tubular atrophy, interstitial inflammation, fibrosis and frequency of fibrointimal hyperplasia. Tubular and interstitial lipid also increase with age, and this lesion may be unique to domestic cats.
 - Abstract: McLeland SM, Quimby JM, Cianciolo RE, Lunn KF, Lulich JP, Herndon AK, Zajic LB. Histologic assessment of the aging feline kidney in cats without kidney disease. Presented at American College of Veterinary Internal Medicine Forum 2019. Poster Presentation. This paper is currently being prepared for publication by Dr. McLeland and will be submitted by the end of the year.
 - Dr. Shannon McLeland is a cat loving board-certified anatomic pathologist who collaborates with our research group from her home in Minnesota, having previously completed a PhD on feline CKD at Colorado State University under the direction of Dr. Quimby.

- *Serum and fecal amino acid profiles in cats with chronic kidney disease*
 - CKD is associated with dysrexia, weight loss, cachexia, and accumulation of harmful metabolites of protein fermentation by colonic bacteria. Amino acid derangements may be a therapeutic target in CKD cats to reduce loss of muscle mass. The objective of this study was to measure serum amino acid concentrations in cats with CKD and compare results to healthy senior cats. We documented that CKD cats had significantly decreased concentration of several essential amino acids and this profile is suggestive of protein wasting and changes in amino acid metabolism.
 - Abstract: Summers S, Blake A, Quimby JM, Lidbury J, Steiner J, Suchodolski J. Alterations in serum amino acid profiles in cats with chronic kidney disease. Presented at American College of Veterinary Internal Medicine Forum 2020. Poster Presentation. This paper has been submitted for publication.
 - This project is part of continued collaborations with Dr. Stacie Summers at Oregon State University.

The following studies are underway:

- *Evaluation of Quality of Life in Cats with Chronic Kidney Disease*
 - The perception of a cat's quality of life is multifactorial and we know that health has a significant impact. The purpose of this study is to combine medical information from the patient with information collected from a quality of life survey completed by caretakers of cats with CKD in order to identify factors influencing the perception of quality of life. This project utilizes a health related QOL survey previously developed by Jacky Reid at Glasgow University and now available as a commercial assessment tool (Button's Fund has assisted by paying the fees to access this assessment tool). Owners are asked to complete the online survey at the time of a veterinary visit in which labwork is performed.
 - Dr. Sarah Lorbach is the clinician who has been working on this project. The data collection is almost complete and we hope to have data for 2022 ACVIM abstract submission.
- *Untargeted metabolomics in young adult cats, senior cats and cats with CKD*
 - In order to better understand the association between gut dysbiosis and increased production of gut-derived uremic toxins, we need to better understand the functionality of the intestinal microbiome by integrating characterization of the intestinal microbiome with the evaluation of the metabolites produced by the gut microbiome. This project involves performing untargeted metabolomics on a set of serum samples from CKD that we previously examined the microbiome on. This allows us to evaluate the functional consequence of the altered fecal microbiome. This project is part of

continued collaborations with Dr. Stacie Summers at Oregon State University. Samples have been sent off for analysis (Metabolon) and we hope to have data for 2022 ACVIM abstract submission.

- *Fecal bile acids in cats with CKD*
 - Fecal bile acids have been little studied in cats, and may be another biomarker of gut dysbiosis associated with CKD. This project is another collaboration with Dr. Stacie Summers and characterizes the composition of bile acids in cats with CKD as compared to healthy geriatric cats. Sample collection and initial sample analysis is complete and the manuscript is being prepared for publication. Some of the data were presented as an abstract at ACVIM Forum 2020. Secondary data analyses are currently underway (delayed due to COVID) under the direction of Dr. Janessa Winston, an internist who specializes in microbiome and bile acid biology.

- *Assessment of Erythrocyte Fragility in Cats with CKD*
 - Anemia is one of the major complications of CKD, affected 30-65% of feline CKD patients. Although the main contributor to this process is thought to be a decrease in erythropoietin and thus decreased bone marrow stimulation, increased red blood cell (RBC) fragility has also been posed as a mechanism that shortens RBC life span. The aim of this study was to explore the effect of CKD and uremic toxins on the fragility of feline RBC using an osmotic fragility assay.
 - Muning Wang, a veterinary student, participated in the 2020 Summer Scholars supported by Buttons Fund to initiate this project. The data collection for this study is completed and analysis is underway.

- *Biometrics of Feline Chronic Kidney Disease*
 - We have an IACUC protocol for collection of routine labwork (chemistry, CBC, UA, T4, blood pressure) in CKD cats and normal cats to allow us to obtain samples as needed for biobanking and to support the clinicopathologic needs of such studies as the Quality of Life Survey. This also allows owners who may not be able to afford full labwork for their cat to participate in screening for clinical trials.

The following initiatives are starting:

- *Feline Renal Biopsy Initiative*
 - We plan to offer renal biopsy/SDS PAGE analysis by our lab (the International Veterinary Renal Biopsy Service; <https://vet.osu.edu/vmc/international-veterinary-renal-pathology-service-ivrps>) for free for a limited period of time (potentially the next three years) to encourage increased submission of feline samples, including necropsy samples (paired

kidney and urine). Although the renal biopsy service is quite busy we routinely get significantly fewer feline samples. This initiative will allow us to obtain additional materials via kidney donation for biobanking and provide materials for investigation of biomarkers of disease. Analysis by the IVRPS included special stains, EM and IF analysis by a board-certified nephropathologist as well as SDS PAGE urine evaluation and is typically ~\$700 per sample.

- *Effects of Anemia and Hypertension on Echocardiographic Measurements of the Heart in Feline Patients*
 - This prospective data collection initiative will provide incentive for recheck echocardiographs in CKD cats who have been diagnosed and treated for their hypertension or anemia. Dr. Eline Nijveldt, this year's research intern is working on this project (in addition to helping with other current projects). Dr. Nijveldt is interested in cardiology and has already been accepted to the cardiology residency here at OSU based on her stellar performance so far this year! We will continue these collaborations with the cardiology service in the future and hope to build a valuable database for future study.

Dissemination

Dr. Quimby is an international speaker and key opinion leader focusing on feline medicine and chronic kidney disease in particular. She seeks to increase awareness of research needs for chronic kidney disease as well as provide updates on recent studies to disseminate information obtained by the program and speaks at several national and international conferences a year.

This year at the American College of Veterinary Internal Medicine (ACVIM) Forum the following abstracts supported by Buttons Fund were presented (presenting author is underlined):

- Paschall R, Quimby JM, Cianciolo RE, McLeland SM, Lunn KF, Elliott J. Assessment of capillary rarefaction in cats with and without CKD. Presented at American College of Veterinary Internal Medicine Forum 2021 (COVID online). Poster presentation.
- Lorbach SK, Quimby JM, Brusach KK, Kinsella H, Toribio R. Ghrelin sample storage and stability in healthy cats. Presented at American College of Veterinary Internal Medicine Forum 2021 (COVID online). Poster presentation.

Awards

Dr. Quimby was elected to the International Renal Interest Society (IRIS) Board. The mission of IRIS is to help veterinary practitioners better diagnose, understand and treat renal disease. (<http://iris-kidney.com/>)