

## **Buttons Fund for Feline Chronic Kidney Disease Research Annual Report 2023**

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.

Website: <https://u.osu.edu/felinekidneyresearch/>

### **Current Fund Vision**

- One of the major aims of the fund is to support clinical studies for CKD cats, typically ranging from \$10,000-45,000 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 mentor young doctors (interns and residents) in their involvement in feline clinical trials. Currently six young doctors are participating in projects supported by Buttons Fund. Support of these research studies promotes interest in feline clinical trials and helps residents meet the publication requirement for board certification in small animal internal medicine.
- These opportunities enhance understanding of interacting with cats in a clinical trials setting, and the importance of advancing feline medicine.
- Our future vision is to continue the feline research intern experience, as well as attracting Master's and PhD student candidates. These positions range from \$55,000-75,000 a year in salary support and can be fully or partially supported by the fund.

### **Studies Supported By Buttons Fund in 2023**

**The following studies have been completed:**

- ***Quantifying defecation frequency between cats with and without chronic kidney disease***
  - This study utilized the Petivity litter box monitoring device to document defecation frequency in cats with and without CKD. Cats with CKD were observed to have significantly more days of missed defecations than normal cats, consistent with

- subclinical constipation. This device will be valuable as a monitoring tool and this study will form the groundwork for a series of studies on therapies for constipation in CKD.
- Zach George is a veterinary student interested in internal medicine who took part in the 2023 Student Scholar program supported by Buttons Fund. He coordinated enrollment for the study, data organization and analysis.
  - *Abstract:* George Z, Quimby J, Jones S, Brusach K, Rudinsky A. Quantifying defecation frequency between cats with and without chronic kidney disease. Zach presented the preliminary results of his study at the National Veterinary Student Scholars Symposium in Puerto Rico, August 2023. We also plan to submit an ACVIM Forum 2024 abstract.
  - *Publication:* manuscript on progress
- ***Assessment of the Effect of Gabapentin on Blood Pressure in Cats with and without Chronic Kidney Disease***
    - Gabapentin is commonly used in feline patients for reducing anxiety during veterinary visits. However its effect on blood pressure has not been systematically assessed and anecdotal reports indicated a potential concern in cats with CKD, possibly due to renal elimination of the drug. This study assessed the effect of gabapentin in a placebo-controlled clinical study in cats with and without CKD. Both groups of cats had a significant decrease in blood pressure after administration of a single dose of 10 mg/kg gabapentin. These results will have important implications for interpreting blood pressure in these patients. This study was partially funded by Everycat Health Foundation and the remnant by Buttons Fund.
    - *Abstract:* Quimby JM, Jones S, Saffire A, Brusach K, Kurdziel K, George Z, Paschall R, Aarnes T. Assessment of the effect of gabapentin on blood pressure in cats with and without chronic kidney disease. Presented at American College of Veterinary Internal Medicine Forum 2023, Philadelphia, PA. Research Report presentation.
    - *Publication:* Manuscript submitted for publication
- ***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 involved performing untargeted metabolomics on a set of serum samples from cats with CKD for whom we previously had described the microbiome. 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.
    - *Abstract:* Summers S, Quimby JM, Winston J. Untargeted metabolomic profiling of serum from cats with chronic kidney disease. American College of Veterinary Internal Medicine Forum 2022.

- *Publication:* manuscript submitted to Scientific Reports
- ***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). Caretakers were asked to complete the online survey at the time of a veterinary visit in which labwork is performed. This study demonstrated that several factors, including severity of disease, anemia, constipation and muscle condition were associated with a decrease QOL score. Further statistical analysis by collaborators at the University of Glasgow confirmed these findings and the data are now ready for publication.
  - Dr. Sarah Lorbach is the internal medicine resident who worked on this project. She was Dr. Quimby's research intern prior to starting her residency.
  - *Abstract:* Lorbach S, Quimby JM, Nijveldt E, Paschall R, Reid J. Evaluation of health-related quality of life in cats with chronic kidney disease. American College of Veterinary Internal Medicine Forum 2022.
  - *Publication:* manuscript in progress
- ***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.
  - *Publication:* manuscript in progress
- ***To sample or not to sample: capturing feline fecal microbiome changes with high-frequency sample collection***
  - In order to study the feline microbiome, it is necessary to better understand how best to collect representative samples. This study looks at sample frequency to determine how

many samples are necessary for an accurate assessment. It was found that more than one sample is ideal to accurately describe a cat's microbiome.

- Dr. Nora Jean Nealon who is Dr. Jenessa Winston's post-doctoral research fellow and has significant microbiome experience spearheaded this project.
- *Abstract:* Nealon NJ, Klein H, Salerno M, Rudinsky A, Quimby JM, Parker V, Howard J, Winston J. To sample or not to sample: capturing feline fecal microbiome changes with high-frequency sample collection. American College of Veterinary Internal Medicine Forum 2022.
- *Publication:* manuscript in progress

**The following studies are underway:**

- ***Feline CKD CARE Study (Caregiver Assessment, Reflection on Experience)***
  - Cats with CKD commonly require long term supportive care with a variety of therapies to manage the complications of their disease. Caregiver burden may play a role in CKD and this survey study aims to describe the experience of individuals who care for a cat with CKD. The goal of this study is to gather information that might prove useful in improving support for the caregiver as well as advancing management strategies for feline CKD.
  - Dr. Lina Lim, who is the 2023 research intern, and will be starting a combined small animal internal residency/PhD program in 2024 will be working on this project.
- ***Effect of Porus One on Reducing Uremic Toxins in Cats with Naturally Occurring CKD***
  - Due to decreased elimination by the kidney, cats with CKD have an increase in uremic toxins such as indoxyl sulfate and these substances have known deleterious effects. Porus One is a carbon-based agent that is thought to bind indoxyl sulfate precursors in the gut and results in decreased systemic concentrations of uremic toxins. This study assessed uremic toxins concentrations after administration of Porus One to client-owned cats with CKD in a placebo-controlled cross-over study. This is a collaboration with Dr. Audrey Cook at Texas A&M University.
  - Dr. Rene Paschall has completed Dr. Quimby's research internship, a rotating internship and is currently an internal medicine resident. She currently is coordinating patient enrollment for the study and to organize and analyze the data from the study.
- ***Evaluation of leptin as a marker of appetite dysregulation in cats with and without CKD***
  - Appetite regulation is complex and involves a balance of orexigenic (appetite-stimulating) and anorexigenic (satiety-inducing) substances. Acylated (active) ghrelin is the main orexigenic hormone, while desacyl (inactive) ghrelin and leptin have been

- found to be anorexigenic. Leptin relies on renal elimination. As a result, accumulation can occur when kidney disease is present due to decreased GFR. This study has been concentrating on optimizing methods of measuring leptin in cats and will then compare concentrations between cats with CKD and normal cats.
- PhD student Katelyn Brusach has been working on optimization of these assays.
  - ***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 is currently underway under the direction of PhD student Dr. John Rowe and PI Dr. Jenessa Winston, an internist who specializes in microbiome and bile acid biology.
  - ***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.
  - ***Feline Renal Biopsy Initiative***
    - We offer renal biopsy/SDS PAGE analysis by 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.

## Dissemination

### Recent publications supported by Button's Fund:

1. Brusach K, Lorbach S, **Quimby JM**, Nijveldt E, Paschall R, Kinsella H, Parker V, Toribio R. Measurement of ghrelin as a marker of appetite dysregulation in cats with and without chronic kidney disease. *Vet Sci* 2023; 10: 464. doi.org/10.3390/vetsci10070464
2. Nealon NJ, Wood A, Klein H, Rudinsky A, Salerno M, **Quimby JM**, Parker V, Howard J, Winston J. The impact of fecal identification markers on the feline microbiome. *Frontiers Vet Sci*. 2023 Feb 8;10:1039931. doi: 10.3389/fvets.2023.1039931.
3. Paschall R, **Quimby JM**, Cianciolo RE, McLeland SM, Lunn KF, Elliott J. Assessment of capillary rarefaction in cats with and without CKD. *J Vet Int Med*. 2023; 37:556-566. doi: 10.1111/jvim.16656.
4. **Quimby JM**, Mclceland SM, Cianciolo RE, Lunn KF, Lulich JP, Erickson AE, Zajic L. Frequency of histologic lesions in the kidney of cats without kidney disease. *J Fel Med Surg* 2022; 24: e472-e480. doi: 10.1177/1098612X221123768
5. Uematsu S, **Quimby JM**, Summers S. Effect of audible static on blood pressure measurement by Doppler ultrasonic sphygmomanometry in cats. *J Fel Med Surg* 2023: doi: 10.1177/1098612X231197084. (Publication costs paid for by Button's Fund)
6. Summers S, **Quimby J**, Gagne J, Lappin M. The effect of dietary protein concentration on the fecal microbiome and serum concentrations of gut-derived uremic toxins in healthy adult cats. *Vet Sci* 2023; 10: 497. doi: 10.3390/vetsci10080497 (Publication costs paid for by Button's Fund)

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 multiple national and international conferences a year.