PennVet
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STUDENT RESEARCH DAY

2026

MARCH 27, 2026

University of Pennsylvania School of Veterinary Medicine

Vernon & Shirley Hill Pavilion

CONTENTS

POSTER SLAM VOTING

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COVER PHOTOS (LEFT TO RIGHT)

1. Gilly having ear temperature measured. Submitted by Tess DeMarro. Photo credit: Penn Vet Working Dog Center Research Team
2. Award winners from Student Research Day 2025. Photo credit: John Donges
3. Porcine electroanatomical mapping procedure. Submitted by Casey Webb.

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PROGRAM

11:15 a.m.	**BOXED LUNCHES AND REGISTRATION**	H132 & Hill Lobby
12:00 p.m.	**OPENING REMARKS**	H130 Marookian Auditorium Andrew M. Hoffman, DVM, DVSc *The Gilbert S. Kahn Dean of Veterinary Medicine* Michael J. May, PhD *Chair, Student Research Day Organizing Committee*
12:15 p.m.	**STUDENT PRESENTATIONS** (10 min with 5 min Q & A) *Introduction of short-term project oral presenters*	H130 Marookian Auditorium Introduction by Caroline O'Rourke
12:20 p.m.	*A comparison of sow behavioral response after intradermal or intramuscular vaccination* Mentor: Dr. Meghann Pierdon	Logan Griggs
12:35 p.m.	*Control of YAP/TAZ signaling on macrophage function during bone healing* Mentors: Drs. Joel Boerckel and George Kotsaris	Ana Mongil
12:50 p.m.	*Assessment of the effect of probiotics on the calf microbiome through the preweaning period* Mentors: Dr. Dipti Pitta and Alexander Post	Jacquelin Spring
1:05 p.m.	**BREAK**	Hill Lobby
1:30 p.m.	**THE CLASS OF 1966 ENDOWED LECTURE** *Redirecting cellular traffic: Translating cell biology into therapeutic opportunities* **Aimee L. Edinger, VMD, PhD** Professor and Faculty Innovation Fellow Developmental & Cell Biology Charlie Dunlop School of Biological Sciences *University of California, Irvine*	H130 Marookian Auditorium 40 min with 10 min Q & A Introduction by Jennifer A. Punt, VMD, PhD
2:25 p.m.	**POSTER SESSION** **Poster Slam** **Poster Crawl** **3:00-3:30 p.m.** Session I: Odd-numbered posters **3:30-4:00 p.m.** Session II: Even-numbered posters	Moderation by Andrew J. Modzelewski, PhD H130 Marookian Auditorium Hill Lobby

PROGRAM CONT'D.

4:00 p.m.	**STUDENT PRESENTATIONS** (10 min with 5 min Q & A) *Introduction of long-term project oral presenters*	H130 Marookian Auditorium Introduction by Caroline Davis
4:05 p.m.	*A short tail: Cytoplasmic tail modifications of an HIV env immunogen to enhance cell surface expression and vaccine immunogenicity* Mentors: Drs. Edward Kreider and Drew Weissman	Breezy Brock
4:20 p.m.	*Investigating unique intestinal epithelial cell states that arise during chronic inflammation* Mentor: Dr. Kathryn Hamilton	Daana Roach
4:35 p.m.	*Investigating changes to the canine gut microbiome in the shelter setting* Mentors: Drs. Brittany Watson, Chelsea Reinhard, and Lauren Powell	Holly Yost
4:50 p.m.	**AWARDS AND RECEPTION** Awards and prizes presented by **Dr. Phillip Scott,** Vice Dean for Research and Academic Resources, **Dr. Andrew Modzelewski, Caroline Davis,** and **Caroline O'Rourke**	H130 Marookian Auditorium and Hill Lobby

THE CLASS OF 1966 ENDOWED LECTURE

IN 1991, A GIFT FROM THE CLASS OF 1966 ESTABLISHED AN ENDOWED FUND TO SUPPORT MAJOR LECTURES AT THE SCHOOL OF VETERINARY MEDICINE.

Aimee L. Edinger, VMD, PhD

AIMEE L. EDINGER, VMD, PhD

Professor and Faculty Innovation Fellow, Developmental & Cell Biology
Charlie Dunlop School of Biological Sciences
University of California, Irvine

Redirecting Cellular Traffic: Translating Cell Biology Into Therapeutic Opportunities

Abstract

Using sphingolipids as an entry point, my laboratory has uncovered evolutionarily conserved mechanisms that redirect intracellular traffic to reprogram cellular physiology under stress. We have shown that small molecules modeled on natural sphingolipids reroute vesicular and nuclear trafficking pathways to modulate nutrient access, mitochondrial function, and growth-associated transcription and signaling. In animal models, these compounds suppress pathological growth programs, overcome drug resistance, restore mitochondrial health, disrupt viral entry, and even enhance delivery of nucleic acid–based therapeutics. By integrating cell biology, chemistry, and a focus on unmet needs in medicine, our work illustrates how cell biologists can produce drugs that are both safe and effective by copying nature.

About Dr. Edinger

Aimee L. Edinger, VMD, PhD, is a professor of developmental and cell biology in the Charlie Dunlop School of Biological Sciences at UC Irvine (UCI), with an adjunct appointment in pharmaceutical sciences. She received a BS in animal physiology from UC Davis and then completed her VMD/PhD at the University of Pennsylvania from 1992–1999. After a postdoctoral fellowship in Craig Thompson's lab at Penn, she joined UCI in 2005. Dr. Edinger's laboratory conducts translational cell biology research focused on altering endolysosomal trafficking to develop new treatments that overcome drug resistance in cancer, correct metabolic defects in obesity, restrict viral replication, and enhance the delivery of nucleic acid therapeutics. Dr. Edinger is an AAAS Fellow, a former UCI Chancellor's Fellow, and a UCI Faculty Innovation Fellow. She is an inventor on seven patents and co-founded a company with her chemistry collaborator that secured multiple NIH Small Business Innovation Research grants as well as venture funding. She is also a committed teacher and mentor, recognized by the De Gallow UCI Professor of the Year Award, two Chancellor's Awards for Excellence in Undergraduate Research, and the Carol Connor Mentoring Award. She currently serves as co-director of an NCI T32 program supporting interdisciplinary cancer research training.

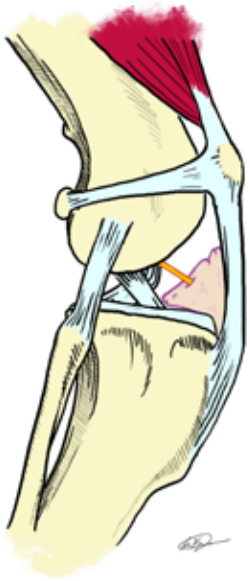
ACKNOWLEDGMENTS

THE UNIVERSITY OF PENNSYLVANIA SCHOOL OF VETERINARY MEDICINE IS GRATEFUL TO THE SPONSORS, DONORS, AND FAMILIES OF ITS PATIENTS WHO MAKE RESEARCH POSSIBLE.

NIH/Boehringer Ingelheim Summer Research Program
We acknowledge the NIH/Boehringer Ingelheim Summer Research Program, which is designed to expose students in their first or second year of veterinary school to all phases of biomedical research.

Richard O. Davies Fund
Established in 2007 by former students and colleagues of Dr. Richard O. Davies, this fund provides support for an award or fellowship to be given at the discretion of the Department of Biomedical Sciences.

The Class of 1966 Endowed Lectureship
A gift from the Class of 1966 established an endowed fund in 1991 to aid and support major annual lectures at the School of Veterinary Medicine.



PHOTOS

THIS PAGE (TOP TO BOTTOM)

1. Submitted by Lucie Pascarosa. Photo credit: Brooke Ezzo
2. Rendition of the ligaments of the right canine stifle, featuring the ligamentum mucosum (orange) coursing from the femoral intercondylar notch to the infrapatellar fat pad. No generative AI was used to create this image. Submitted by Nathan Ko.
3. Vauk completing voluntary head dunks. Submitted by Tess DeMarro. Photo credit: Penn Vet Working Dog Center Research Team

FACING PAGE (CLOCKWISE FROM TOP RIGHT)

1. VMD-PhD student Katherine Morucci in Canchayllo, Junin, Peru during a run-in with a friendly alpaca. Submitted by Katherine Morucci.
2. GPS-collared dog in a study of free-roaming dogs in Peru. Submitted by Katherine Morucci.
3. Mouse intestinal epithelium after induced-colitis with DSS. ECAD in purple, MHC II (I-A/I-E) in orange, LCN2 in red, DAPI in light blue. Scale bar = 50 um. Image taken on Zeiss LSM980 and processed in ImageJ/Fiji platform. Submitted by Daana Roach.
4. Penny completing head towel intervention. Submitted by Tess DeMarro. Photo credit: Penn Vet Working Dog Center Research Team

SPECIAL THANKS

Organizing Committee

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Michael J. May, PhD

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STUDENTS
Caroline Davis
Caroline O'Rourke
Lola Uliano

Abstract and Poster Judging

ABSTRACT AND POSTER JUDGES
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Stephen D. Cole, VMD, DACVM
Roderick B. Gagne, PhD
Thomas D. Parsons, VMD, PhD
Darko Stefanovski, PhD
Brittany Watson, VMD, PhD, DACVPM

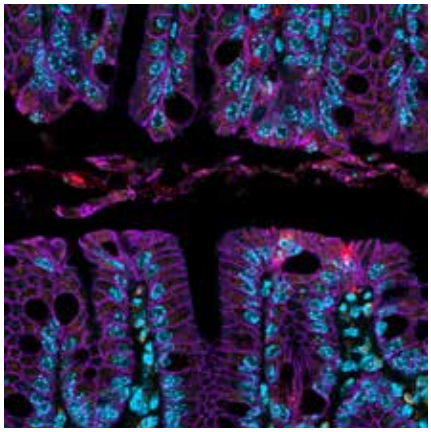
Thank you

Heartfelt thanks to **Dr. Kathryn E. Michel** for her foundational role in establishing and growing Student Research Day, and to **Dr. Amy Durham** for continuing to ensure that the event has dedicated time in the school calendar.

We are grateful to **Dr. Christopher J. Lengner**, Chair, Department of Biomedical Sciences, for generously making the Richard O. Davies Fund available to support student awards.

Sincere thanks to **Dr. Jenni Punt** for her generous donation establishing cash prizes for the Poster Slam.

We also thank **Sue Waddington-Pilder, Stephen Hawkins, Steven Atchison, Haneef Herring, Rachael Keith, Penn Vet Communications, Penn Vet Facilities Services**, and **Penn Vet Information Technology** for their invaluable organizational, technological, photographic, promotional, and logistical support.



PHI ZETA

Phi Zeta was founded in 1925 by a group of senior veterinary students in the New York State Veterinary College at Cornell University. With the assistance of a group of faculty members, including the dean of the college, Dr. Veranus A. Moore, the Society was formally organized, and Dean Moore was elected as the first president of the Alpha Chapter. The Society of Phi Zeta was organized in 1929 at a meeting in Detroit, Michigan, and Dean Moore became the first president of the Society. Also, in 1929, a charter was granted to the School of Veterinary Medicine at the University of Pennsylvania, and the Beta Chapter was established. In 1931, the Executive Committee approved the petition of a group from Iowa State College, and the Gamma Chapter was established. Since then, thirty chapters have been chartered, bringing the total number of chapters to thirty-three. Chapters of the Society may be formed at any recognized veterinary medical college or at any other institution of higher learning.

NAME AND SYMBOLS OF THE SOCIETY

The organizers of the Society, when seeking a suitable name, sought the help of a learned Greek scholar, Professor George P. Bristol of Cornell University. Professor Bristol suggested a Greek word, which in the Latin form is spelled PHILOZOI and means "love for animals." The abbreviation of Phi Zeta was adopted as the name of the Society.

The emblem consists of a pendant formed by the letter Phi superimposed on the letter Zeta. The design was the work of Louis Agassiz Fuertes, the great naturalist and artist.

UNIVERSITY OF PENNSYLVANIA OFFICERS

Beta Chapter
Dr. Margret Casal, President

CLASS OF 2027

Zoe Araujo, Susannah Epstein-Boley, Elizabeth Fiepke, Colleen Geldermann, Audrey Griffith, Kenzie Milne, Ana Mongil, Kacie North, Gianna Rubel, Sarah Solomon, Daelyn Stabler, Sofia Vonderheyde

CLASS OF 2026

Elena Anderson, Mariane Ball, Christopher Brown, Jessica Browne, Zach Cochran, Taylor Dube, Lindsay Gelb, Georgia Giannaras, Zoe Goldberg, Nicholas Laganelli, Keara Monaghan, Alexandra Thomson, Caroline Zagoren

INDUCTED AS JUNIORS (V'26)

Hannah Anderson, Theresa Astmann, Jack Aversa, Jordan Brofsky, Krista Colussi, Courtney Cosgrove, Emily DeCicco, Natalie Durant, Sabrina Garcia, Laura Grant, Abigail Hamilton, Alison Kowalski, Ragan Kules, Morgan Lazar, Madison Lofgren, Julie Rosta, Casey Rubin, Julianne Sheehan, Jordan Stoltz

STUDENT RESEARCH DAY BINGO

NAME _____

2026 Student Research Day BINGO CARD

Check in at registration desk *stamp*	**Attend a short-term talk** *stamp*	**Attend the keynote lecture** *stamp*	**Attend a long-term talk** *stamp*
Meet a 2nd year vet student	**Meet a VMD-PhD student**	**Meet a clinical year vet student**	**Meet a faculty advisor**
Ask a poster presenter about their methods	**Ask a poster presenter about their future directions**	**Vote for your favorite Poster Slam presenter by 4:15PM**	**Compliment someone on their hard work!**

- **Submit** your completed sheet (with stamps) to a student coordinator (Lola Uliano, Caroline Davis, or Caroline O'Rourke) before the Awards Ceremony
- **BE PRESENT** at the drawing **(H130, during Awards Ceremony)**

Complete the top row to be eligible for the prize drawing.

PRIZES

Dog Skeleton Model

Keurig K-Mini Go Coffee Maker

PowerXL Vortex Pro Air Fryer

HOW TO PLAY

1. Everyone is welcome to play, but **only Penn Vet students are eligible to win prizes**.
2. Pick up a bingo card at the registration desk.
3. To be eligible for the prize drawing, collect stamps for **all four squares in the top row**. Completing the remaining squares is optional but encouraged.
4. Stamps can be obtained from the student coordinators: **Caroline Davis, Caroline O'Rourke,** and **Lola Uliano**.
5. **Before the awards ceremony (4:50 p.m.)**, Penn Vet students who have completed the top row should submit their bingo card to a student coordinator to be entered into the drawing. **Be sure to write your name at the top of the card**.
6. Players **must be present at the drawing during the awards ceremony** to win.

ABSTRACT NUMBERS

Abstracts are ordered alphabetically by the presenting student's last name.

Oral Presentations: Indicated by an asterisk*

Poster Presentations: Abstract numbers correspond to the poster board number.

1. Theresa J. Astmann
2. Xuechen Bai
3. Lindsay Bomba
4. Breezy Brock*
5. Kerry Campbell
6. Tess DeMarro
7. Erin K. DeNardo
8. Ava Ehrlich
9. Amanda Girgis
10. Veronica Gordon
11. Logan Griggs*
12. Mackensie Gross
13. Edward Hallam
14. Sara Hernández Suárez
15. Emily Hughes
16. Rachael Keith
17. Nathan T. Ko
18. Isabella Lozano
19. Ramit Manhas
20. Megan McCarthy
21. Ana Mongil*
22. Katherine Morucci
23. Skyler Murphy
24. Lucie Pascarosa
25. Raegan J. Petch
26. Margaret Piecz
27. Hayley Piper
28. Isel Pollock
29. Toni I. Rabasco
30. Jenna Raffael
31. Daana M. Roach*
32. Owain Rose
33. Morgan Simms
34. Jacquelin Spring*
35. Emmalyn Tavani
36. Advika Thandoni
37. Jacob Tollinsky
38. Rebecca Turner
39. Lola L. Uliano
40. Kristen Walsh
41. Casey Webb
42. Anne K. Yauch
43. Holly Yost*

ABSTRACTS

Abstracts are ordered alphabetically by the presenting student's last name.

1. EXPLORING GAPS1-MEDIATED ANTIPHAGE IMMUNITY IN KLEBSIELLA PNEUMONIAE.

Theresa J. Astmann, Chrishan Fernando, Greater Oyejobi, Jorge L. Rodriguez, and Nicole D. Marino.

Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

Klebsiella pneumoniae (KP) is a major opportunistic pathogen and a leading cause of hospital-acquired pneumonia, sepsis, and other invasive infections. The rapid emergence of hypervirulent and multidrug-resistant lineages has made KP infections the third leading cause of antimicrobial resistance-associated mortality worldwide. Although phage therapy has successfully cleared many drug-resistant KP infections, clinical outcomes remain highly variable. This variability is due in part to the diverse repertoire of antiphage systems encoded in KP genomes. Here, we identify and characterize GAPS1 (GMT-encoded anti-phage system 1) as one of the top ten most abundant antiphage systems in KP. Notably, GAPS1 is enriched in high-risk sequence types (ST 11 and 258) that are strongly associated with hospital outbreaks and the global dissemination of carbapenem resistance. We show that GAPS1 confers robust immunity against multiple families of *Klebsiella* and *E. coli* phages. This defense depends on the conserved PD-(D/E)xK nuclease domain, as mutating these active site residues abrogates antiphage activity. Challenging GAPS1-expressing cells with high titers of phage triggers growth arrest, suggesting that GAPS1 may halt viral replication by non-specifically targeting cellular components. To investigate how phages overcome GAPS1 immunity, we structurally modeled potential interactions between GAPS1 and proteins encoded in variable regions of *Klebsiella* phage genomes. This approach can uncover novel phage-encoded inhibitors for GAPS1 and other antiphage systems in KP. Together, our findings establish GAPS1 as a prevalent and potent antiphage defense in clinically relevant KP lineages and provide a framework for systematically uncovering phage counter-defenses that can improve the success of phage therapeutics.

Research Grant: National Institutes of Health General Medical Sciences (R00GM143476)

2. CROSSTALK BETWEEN MACROPHAGES AND FAP-CAR T CELLS IN FIBROTIC MATRICES.

Xuechen Bai[1], Henry Utset[2], and Ellen Puré[3].

[1]School of Veterinary Medicine, University of Pennsylvania; [2]Perelman School of Medicine, University of Pennsylvania, Medical Scientist Training Program; [3]Department of Biomedical Sciences, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

Background: Idiopathic pulmonary fibrosis (IPF) is marked by excessive extracellular matrix (ECM) deposition driven by fibroblast activation and immune dysregulation. Fibroblast activation protein-targeted (FAP-) CAR T cells have been proposed as an antifibrotic therapy, but their interactions with macrophages remain unclear.

Methods: Fibroblast-derived matrix cultures (FMCs) from IPF fibroblasts were treated with FAP-CAR T cells, non-transduced (NTD) T cells, macrophages, or combinations. Macrophage polarization, ECM remodeling, fibroblast markers, and cytokine secretion were assessed by immunofluorescence, second-harmonic generation (SHG) imaging, collagen-hybridizing peptide (CHP) staining, and ELISA.

Results: FAP-CAR T cells reduced $CD206^+$ (M2-like) and increased $CD86^+$ (M1-like) macrophages, indicating a polarization

shift. IFN-γ was detected only in FAP-CAR groups and was further elevated with macrophages, whereas TNF-α was absent. COL1 staining and SHG showed little change, but CHP staining revealed reduced denatured collagen with FAP-CAR treatment, further decreased by macrophage co-culture. Fibroblast markers (vimentin, CD90, FAP) showed modest reductions, suggesting limited direct depletion.

Conclusion: FAP-CAR T cells modulate the fibrotic microenvironment by shifting macrophage phenotypes, increasing IFN-γ, and enhancing collagen clearance in concert with macrophages, while exerting modest effects on fibroblast killing. These findings provide insight into immune–fibroblast interactions in IPF and support the potential of FAP-CAR–based antifibrotic strategies.

3. REFINING THE ANESTHESIA OF NEONATAL MICE.

Lindsay Bomba[1] and James O. Marx[2].

[1]School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA; [2]University Laboratory Animal Resources, Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

Neonatal mice are often anesthetized in research. Despite this, there is a lack of published guidance on the best anesthetic methods for these animals. Isoflurane administration is often based on anecdotal evidence and there are concerns about the distress of anesthesia using hypothermia. The objective of this study is to assess the efficacy and distress of isoflurane and hypothermia anesthesia to achieve a surgical plane of anesthesia in neonatal mice. Post natal day (PND) 1 (n=6), 4 (n=5), 7 (n=4) and 14 (n=7) mice were induced with 4% isoflurane, then maintained at increasing concentrations of isoflurane for 10-15 minutes each. The anesthetic depth was then assessed based on the response to a noxious stimulus. PND 1 (n=6) mice were anesthetized by hypothermia by placing them in a nitrile glove and submerging them in an ice-water bath for 8 minutes. PND 1, 4 and 75% of PND 7 mice did not reach a surgical plane of anesthesia using isoflurane. Additionally, significant respiratory rate depression was noted in all of the mice. 100% of PND 14 mice achieved a surgical plane of anesthesia on isoflurane, with a minimum alveolar concentration of 2.6 ± 0.4%. Using hypothermia, 100% of PND 1 mice reached a surgical plane of anesthesia for 4.6 ± 1.2 minutes and had a 100% survival rate. Hypothermia induction appears to be more distressing than isoflurane. We conclude that isoflurane is not an effective anesthetic for achieving a surgical plane in neonatal mice until PND 14. Hypothermia is a safe and effective way to achieve a surgical plane of anesthesia in PND 1 mice. Further work is in progress to analyze effective anesthetic methods in PND 4 and 7 mice.

Research Grant: TransnetYX

Student Support: NIH/Boehringer Ingelheim

ORAL PRESENTATION

4. A SHORT TAIL: CYTOPLASMIC TAIL MODIFICATIONS OF AN HIV ENV IMMUNOGEN TO ENHANCE CELL SURFACE EXPRESSION AND VACCINE IMMUNOGENICITY.

Breezy Brock[1], Natalia Perez[1], Houping Ni[1], Beatrice H. Hahn[1], Pamela J. Bjorkman[2], James Hoxie[1], Drew Weissman[1], and Edward F. Kreider[1].

[1]University of Pennsylvania, Philadelphia, PA; [2]Caltech, Pasadena, CA.

The HIV Envelope protein (Env) is a central target in HIV vaccine design, yet intrinsic features limit antigen availability, motivating immunogen engineering strategies. During natural infection, Env surface expression is tightly regulated by internalization motifs (GYxxΦ) within its long cytoplasmic tail (CT). While advantageous for viral replication, this mechanism limits Env availability for immune recognition in vaccine contexts. Our lab has previously found that disrupting this motif (ΔGY/Y712I) and incorporation of a truncated HIV/SIV chimeric CT increased surface Env and IgG titers following immunization (SIV.CT). Additional infection-based studies have identified mutations (S727P and R722G) in the CT that further enhance Env surface expression. Here we introduced those viral mutations into our SIV. CT mRNA-encoded Env immunogens containing a disrupted GYxxΦ motif (ΔGY/Y712I). HEK 293F cells were transfected with mRNA constructs and cell surface expression was analyzed via flow cytometry using a panel of conformationally dependent monoclonal antibodies. mRNA constructs were then formulated into lipid nanoparticles and used to vaccinate BALB/c mice intramuscularly at weeks 0 and 4 at a 0.8μg dose. Serum drawn at weeks 3 and 6 post prime were evaluated using autologous ELISA assays. All CT modifications resulted in a ~1 log increase in Env cell surface expression relative to the wild-type (WT) Env (measured via mean fluorescence intensity), with S727P-containing variants consistently achieving the highest expression independent of the GYxxΦ deletion strategy (Y712I, S727P vs. Y712I and ΔGY, Y712I vs. ΔGY Fold over Mock: 404 vs. 340 and 380 vs. 285). Following homologous boost, S727P-containing variants elicited ~ 2.5-3-fold higher antibody binding compared to WT at 6 weeks post-prime (Y712I/S727P vs. WT geomean AUC: 217,749 vs.86,932, geomean end point titer: 375,250 vs. 130,190). These findings identify S727P-containing CT variants as optimal candidates for enhancing Env surface expression without sacrificing conformation integrity.

5. PREVALENCE OF LPDV AND REV IN PENNSYLVANIA AND NEW JERSEY WILD TURKEYS (MELEAGRIS GALLOPAVO).

Kerry Campbell[1], Ryan Koch[1], Erick Gagne[1], Axel O.G. Hoarau[1], Tryssa de Ruyter[2], Caitlin Duffy[1], Lucie Pascarosa[1], Casey L. Maynard[1], Andrew Cushman[5], Heather Flick[5], Anthony Musselman[5], Julianna Patsko[5], Rachel Bealer[5], Graham Rhone[5], Mary Jo Casalena[5], Andrew Di Salvo[5], Ken Duren[5], Jay T. Armstrong[3], Frances E. Buderman[4], R. Scott Larsen[1], Caroline Sobotyk[3], Erica A. Miller[1], Kevin D. Niedringhaus[1], Brock Geary[1], and Eman Anis[1].

[1]Department of Pathobiology, Wildlife Futures Program, School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA; [2]Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA; [3]Department of Pathobiology, University of Pennsylvania, Philadelphia, PA; [4]Department of Ecosystem Sciences and Management, Pennsylvania State University, University Park, PA; [5]Pennsylvania Game Commission, Harrisburg, PA.

Lymphoproliferative disease virus (LPDV) is an avian retrovirus that has been increasing in prevalence in wild turkeys (*Meleagris gallopavo*) in the United States since 2008. Reticuloendotheliosis virus (REV) is another avian retrovirus that is rare in wild populations, but can have high mortality rates in wild turkeys. The goal of this project was to complete the 4 year turkey health surveillance project that has been tracking changes in LPDV and REV prevalence in Pennsylvania and New Jersey wild turkey populations. The last portion of the project was running the final 131 PA and first 62 NJ wild turkey samples to test for both viruses, as well as compiling data from the past 4 years to put together a cohesive look at the changes in prevalence of LPDV and REV in these wild turkeys. Whole blood that had been collected from turkeys across PA and NJ were used to extract DNA using the DNAeasy Blood and Tissue protocol from Qiagen, followed by PCR to amplify the partial gag and LTR sequences of the LPDV and REV viruses, respectively. Finally, gel electrophoresis was run and analyzed for presence or absence of the viruses in each sample. The 2025 PA samples (n=131) showed an overall 67% prevalence of LPDV across PA regions and a 1% prevalence of REV. This showed a similar trend to what was found in the previous 4 years, which is that LPDV prevalence has remained around 70% (526/756), whereas REV has been

around 1% (7/756) across all regions. New Jersey samples (n=62) showed a lower prevalence than what has been found in PA, with LPDV being 53% and REV being <1%. These results will be used to determine how viral, bacterial, and parasitic coinfections affect wild turkeys, and help Pennsylvania and New Jersey agencies determine best management strategies going forward.

Student Support: Wildlife Futures Program; Pennsylvania Game Commission; Richard King Mellon Foundation

6. HOW COOL IS THAT? EFFECT OF WATER TEMPERATURE AND COOLING METHOD ON CANINE EXERTIONAL HYPERTHERMIA.

Tess DeMarro, Molly Buis, Amritha Mallikarjun, Meghan Ramos, and Cynthia Otto.

Penn Vet Working Dog Center, Department of Clinical Sciences and Advanced Medicine, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

Exertional hyperthermia is a major preventable cause of morbidity and mortality in canine athletes. In a nine-condition crossover study of exertional hyperthermia in 12 working dogs, we tested four 30-second cooling methods: partial water immersion, voluntary head dunk, controlled drinking, and wet head towel, using water at either 72°F or 59°F, compared to passive cooling. Temperature was monitored in three ways: an ingestible pill, a subcutaneous temperature chip, and an ear thermometer. At least nine dogs completed each exercise and cooling intervention. No adverse events were noted. Compliance with the cooling methods and the ear thermometer was variable. When examining all methods of temperature acquisition as a function of cooling method in a multivariate mixed-effects model, partial water immersion was the most effective method, with 59°F water cooling more rapidly than 72°F water. Voluntary head dunk and water consumption both lead to rapid cooling. The water temperature had a limited impact on cooling with the head dunk, but consuming 72°F water led to more rapid cooling than consuming 59°F water. The wet head towel was not an effective alternative to voluntary head dunk. In canine exertional hyperthermia, when signs of heat stress are recognized, activity should be terminated and active cooling initiated. When possible, total or partial immersion in cold water is recommended. Using combinations of voluntary head dunk and controlled cool water consumption also provides a safe, effective, and portable means of active cooling.

Research Grant: American Kennel Club Canine Health Foundation

Student Support: Frank W. Lloyd Research Fellowship

7. INVESTIGATING THE ROLE OF BACTERIAL ARGININE BIOSYNTHESIS IN THE POST-HATCHING LIFE CYCLE OF TRICHURIS MURIS.

Erin K. DeNardo[1], E. Jane Albert Hubbard[2], and Ken Cadwell[1,3,4].

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; [2]Department of Cell Biology, NYU Grossman School of Medicine, New York, NY; [3]Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA; [4]Institute for Immunology and Immune Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA.

The parasitic whipworm *Trichuris* infects an estimated half a billion individuals worldwide and can result in severe gastrointestinal symptoms, weight loss, and growth retardation, with related parasitic species affecting other mammals such as dogs and pigs. *Trichuris* parasitic worms hatch within the mammalian intestine following interactions with the host gut microbiota. Within the intestines, they complete multiple molts prior to releasing immature eggs into the

environment. Adult worms lay thousands of eggs daily which results in a sustained environmental presence and makes them challenging to eradicate. These worms have a complex life cycle that critically depends on interactions with the gut microbiota to facilitate hatching, yet the precise mechanisms governing this and the role of bacteria post-hatching remains poorly understood.

Previous work using *Escherichia coli* as a model implicated bacterial fatty acid biosynthesis in growth and reproductive defects of the mouse parasite *Trichuris muris*. Hybrid metabolomics revealed that lysates from *E. coli* with genetic deletions in fatty acid biosynthesis were unexpectedly low in arginine and ornithine. This project aims to determine the role of bacteria through the post-hatching life stages of *T. muris* and confirm the effects of reduced bacterial arginine biosynthesis on growth and reproductive outcomes in adult worms through germ-free mouse experiments. Here, we confirm the altered reproductive outcomes in mice colonized with arginine biosynthesis mutants. We also evaluate whether the bacterium must be present continuously or only during specific windows of infection, leveraging reversible colonization with an *E. coli* strain with several auxotrophic deletions requiring exogenous supplementation for replication and persistence in the gut.

Research Grant: NIH R01 AI179896-03

Student Support: NIH T32 03AI070077

8. COLITIS-INDUCED DUODENAL ALPHA-SYNUCLEIN EXPRESSION INDEPENDENT OF ApoA1 IN A MOUSE MODEL OF PARKINSON'S DISEASE.

Ava Ehrlich[1], Sromona Das[2], R. Tyler Skrinak[2], Charles Shen[2], and Alice Chen-Plotkin[2].

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Parkinson's Disease (PD) diagnosis relies on clinical symptoms, highlighting the need for biomarkers that enable earlier detection and support therapeutic development. Apolipoprotein A1 (ApoA1) has been identified as a potential biomarker, with higher plasma levels linked to milder disease severity. Evidence suggests that alpha-synuclein (aSyn) pathology, a hallmark of PD, may originate in the gut and spread to the central nervous system via the gut-brain axis. This project aims to investigate whether ApoA1 modulates this transmission and whether gut inflammation enhances aSyn pathology, given the prevalence of gastrointestinal dysfunction in PD patients. We employed a previously established aSyn preformed fibril (PFF) feeding model (Kelvin Luk) in combination with colitis induction using Dextran Sodium Sulfate (DSS). A cohort of 64 wildtype (WT) and ApoA1 knockout (KO) mice was divided into DSS or control groups and further subdivided to receive food infused with either aSyn monomers or PFFs. Six months post-feeding, mice were perfused and tissues harvested. Histological analysis confirmed sustained colitis in DSS-treated mice, with no genotype-specific differences in colitis severity. ELISA for total aSyn revealed a significant increase in aSyn expression in the monomer + DSS group compared to monomer alone, while no significant effects were observed in PFF-fed groups. These findings suggest that inflammation alone may promote aSyn upregulation in the gut, independent of ApoA1 status, highlighting a potential mechanism for gastrointestinal involvement in PD pathology.

9. COMPARATIVE INVESTIGATION OF ULTRA-HIGH DOSE RATE RADIATION THERAPY (FLASH-RT) AND CONVENTIONAL RADIATION THERAPY IN CANINE GLIOMA TUMOR CELLS.

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Glioma is an aggressive form of brain neoplasm that poses a clinical challenge to both canine and human species. Conventional radiation therapy (CONV-RT), part of the standard treatment for glioma, is typically delivered at a dose "rate" of <0.1 Gy/second. In contrast, FLASH radiation therapy (FLASH-RT) is an emerging form of radiation therapy that delivers an ultra-high dose "rate" (> 40 Gy/second) of ionizing radiation to effectively destroy malignant tumors while minimizing damage to healthy tissues. We compared the effects of CONV-RT and FLASH-RT in two canine glioma cell lines, J3T-Bg and G06A. We determined the radiation response via clonogenic assay and cytokine/chemokine production was quantified using Enzyme-Linked Immunosorbent Assays (ELISA). Bulk RNA sequencing was also performed. The J3T-Bg cell line exhibited growth but did not form colonies in the clonogenic assay, whereas the G06A cell line showed colony formation, with the highest plating efficiency (5.7%) at 400 cells per well. Following irradiation, colony formation was observed in cells exposed to 2 Gy of CONV-RT and 4 Gy and 8 Gy of FLASH-RT. ELISA analysis showed interferon gamma (IFN-γ) levels were undetectable in both cell lines, while only J3T-Bg produced measurable C-C motif chemokine 2 (CCL2/MCP-1), trending upward across sham-RT (0 Gy), CONV-RT, and FLASH-RT groups. These results, however, were not statistically significant. Nanodrop RNA quality control confirmed minimal protein contamination (A260/A280 ~2.0), but G06A samples showed potential organic contamination (A260/A230 <1.8).

Research Grant: Dozer Summer Canine Cancer

Student Support: NIH/Boehringer Ingelheim

10. COMPUTED TOMOGRAPHIC DESCRIPTION OF THE PHRENIC LYMPH NODE IN CATS.

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The phrenic lymph node (PLN) is a small lymph node (LN) located within the plica venae cavae, described as part of the dorsal thoracic lymph center in feline, bovine, and equine species. Currently, there is no literature describing the PLN using computed tomography (CT) in cats. The aims of this retrospective study were to describe the CT appearance of PLN in cats and to assess its prevalence in a feline population who underwent thoracic and/or abdominal CT for clinical purposes. The electronic medical records of the Ryan Animal Hospital (University of Pennsylvania) were searched for cats who presented with lymphadenopathy in CT in the period 2013-2022, and for all cats who underwent thoracic and abdominal CT examination in the period 2023-2024. All CT images were reviewed, and size, shape, contrast enhancement of the PLN were recorded, together with final diagnosis and enlargement of other LNs.

The PLN was visible in 12/143 cats with lymphadenopathy. It was rounded in 5 cats, ovoid in 6, fusiform in 1; median diameter was 2.5 mm (range: 1.2-4.6 mm) and contrast enhancement was homogeneous in all cases. Of these 12 cats, 6 were clinically healthy renal donors, 3 had neoplastic and 2 had infectious disease, and one had chylothorax. In

the overall population (2023-2024), the PLN was detected in 10/117 cats (8.5%). In all cats with visible PLN, at least one thoracic or abdominal LN was enlarged.

The PLN in cats can be detected on CT, with a prevalence in this species of 8.5%.

ORAL PRESENTATION

11. A COMPARISON OF SOW BEHAVIORAL RESPONSE AFTER INTRADERMAL OR INTRAMUSCULAR VACCINATION.

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Evaluating vaccination methods is important for improving animal welfare and vaccinator experience, which may enhance compliance with protocols. This study compared behavioral responses of sows vaccinated via intramuscular (IM) or intradermal (ID) routes. Sows and gilts (n = 194) were blocked by parity and randomly assigned to ID (0.2 mL *Sequivity*® via IDAL® device) or IM (1 mL *Sequivity*® via Prima Tech® syringe). ID injections were given at neck, perianal, or udder skin sites; IM injections were in the neck. Vaccinations occurred pre- and post-farrowing, totaling 401 recorded events. Behaviors (flinch, head shake, aggression, retreat, scratching), posture changes, and lying duration were analyzed using mixed-effects models. ID vaccinations (n = 194) were performed on 95 sows (avg parity 1.7), IM on 99 sows (n = 207; avg parity 1.5). Posture change occurred in 27% of ID vs. 38% of IM events (OR = 1.90; P = 0.03). Flinching was more frequent after IM (89%) than ID (64%) (OR = 5.74; P < .001). Aggression (IM: 9.2%; ID: 2.6%) and retreat (IM: 18%; ID: 12%) were also higher for IM (P ≤ 0.03). No differences were observed for head shaking or scratching. Sows vaccinated intradermally spent more time lying post-vaccination (58.5% vs. 45.5%; P = 0.003). IM vaccination elicited stronger negative reactions—flinching, aggression, retreat, and posture changes—while ID vaccination was associated with calmer behavior and longer lying time, suggesting improved welfare. The IDAL device may also enhance vaccinator safety and compliance by reducing adverse sow responses.

Student Support: Pennsylvania Pork Producers Council

12. PRELIMINARY DATA ASSESSING CLINICAL DIFFERENCES AND OUTCOMES BETWEEN ADULT DRAFT BREED HORSES AND NONDRAFT BREEDS PRESENTING FOR ACUTE ABDOMINAL PAIN.

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The objective of this study was to determine whether draft breeds presenting for acute abdominal pain have an increased risk of morbidity and mortality compared with nondraft breeds. This was a retrospective case control study (n=476). Medical records of adult draft horses (n=119) that presented for acute abdominal pain from to November 2016 to October 2025 were reviewed. For each draft case, 3 adult nondraft cases were randomly selected to serve as controls (n=357), based on presenting complaint of acute abdominal pain and timeframe. Pearson's Chi Squared and Kruskal Wallis test were performed; level of significance p<.05. Overall survival to hospital discharge was 81%, with no difference between draft and nondraft breeds. Overall morbidity included postoperative colic (38%), SIRS (29%), fever (28%),

diarrhea (17%), postoperative reflux (12%), surgical site infection (12%), catheter complications (11%), pneumonia (4%), and *Salmonellosis* (2%). There was a significant difference between draft and nondraft breeds and diagnosis category, with draft breed having a higher proportion of gastric lesions and nondraft breeds having a higher proportion of small intestinal strangulating lesions. Draft breeds were more likely to have a longer duration of colic prior to presentation, higher admission peritoneal lactate, lower mean arterial pressure and PaO_2 under anesthesia, post anesthetic upper respiratory obstruction, and longer duration of hospitalization. In our hospital, draft breeds had a significantly higher proportion of gastric lesions compared to nondraft breeds. Aside from a higher proportion of upper respiratory obstruction, draft breeds had no difference in morbidity or mortality as compared with nondraft breeds.

13. FUROSEMIDE AND/OR CLODRONATE EFFECTS ON CIRCULATING BIOMARKERS OF BONE TURNOVER IN THOROUGHBRED HORSES.

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Furosemide (F) and Clodronate (C) have been co-administered to racehorses. In other species, both drugs affect bone turnover and increase fracture risk. Biomarkers provide insight into osteoclast (CTX-I) and osteoblast (OSC) activity. Our objective was to evaluate the effect of F and C on OSC, CTX-I and cytokine gene expression in exercising Thoroughbreds. We hypothesized there would be differences in these biomarkers between horses (n = 16) randomly assigned to receive F (S/F: 1.1 mg/kg IV every 7 days for 12 weeks), C (C/S: 1.8 mg/kg IM C), or a combination of both drugs (C/F) compared to saline (S/S) controls. Whole blood samples were collected up to 84 days after drug administration. Serum and mRNA were stored at -80C until analysis. CTX-I and OSC, and white blood cell mRNA (IL-1 α, IL-R α, IL-2, IL-4, IL-6, IL-10, IL-15, IFNγ, TGF-β2, and TNFα) were evaluated using ELISA and PCR, respectively.

Serum biomarker concentrations were statistically different compared to saline controls at specific time points. CTX-1 was decreased in the C treatment group (S/C) at 3 different time points: days 1, 7 and 48 (P=0.006, 0.005 and 0.019, respectively). OSC was increased at day 0 and decreased on day 84 ($P < 0.01$ and P=0.022) in the F treated group (F/S).

Gene expression of IL-10, IL-1R α, and TGF-β (n = 4 pooled) appeared to decrease for F and C groups whereas IL-1$\alpha\alpha$ expression increased 2 fold in the F treatment group on day 7, compared to day 0. Due to time constraints, samples were pooled for each group. Individual sample processing is needed to confirm these findings.

In summary, this pilot suggests F and C may affect bone metabolism in young exercising Thoroughbreds. Additional studies are warranted to elucidate potential impact on bone growth and development, performance status, and athletic longevity.

14. HARNESSING THE NEUROVASCULATURE FOR PRECISION DRUG DELIVERY INTO THE CNS.

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Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disease of the central nervous system (CNS). While relapsing-remitting MS (RRMS) is characterized by infiltration of peripheral autoreactive immune cells into the CNS, across a disrupted blood-brain barrier (BBB), progressive MS (PMS) presents low-grade "compartmentalized"

neuroinflammation that persists behind a largely intact BBB. This shift in disease biology has limited the effectiveness of existing immunotherapies and represents a central barrier to therapeutic progress. Critically, the mechanisms sustaining this compartmentalized inflammation remain poorly understood, contributing to the lack of effective treatments for PMS. Here, we leveraged a newly developed animal model closely mirroring MS progression together with innovative tools targeting CNS blood vessels to test the hypothesis that the neurovasculature not only sustains compartmentalized neuroinflammation but also serves as a powerful route for targeted therapeutic delivery into inflamed tissues.

We exploited the carrying abilities of lipid nanoparticles (NPs) and engineered them to target the BBB. These NPs were loaded with a potent Bruton tyrosine kinase inhibitor (BTKi), targeting key intracellular pathways in immune cells implicated in PMS pathogenesis. By directing BTKi-loaded NPs to the neurovasculature, we aimed to overcome BBB-associated delivery barriers and achieve precise, localized modulation of neuroinflammation.

Treatment with BTKi-loaded NPs resulted in significant attenuation of clinical disease severity, reduced demyelination and decreased inflammatory infiltrates within the CNS. Importantly, delivery of BTKi reshaped the CNS immune environment, shifting immune cells away from pro-inflammatory states, restoring BBB integrity, and leading to a marked reduction in meningeal B cell aggregation- a key component of compartmentalization in PMS. Together, these findings establish neurovascular-targeted drug delivery as a powerful and adaptable approach that leverages the BBB's role in sustaining neuroinflammation, allowing more precise and efficient delivery of therapeutics to otherwise inaccessible inflammatory niches.

Student Support: NIH T32

15. A NOVEL microRNA AS A POTENTIAL REGULATOR OF THERMOGENESIS AND BIOMARKER FOR OBESITY.

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Obesity is a major global health concern, affecting nearly 30% of adults worldwide and serving as a significant risk factor for numerous chronic health conditions, placing an increasing burden on healthcare systems. Extracellular vesicle (EV)-derived microRNAs (miRNAs) have emerged as key regulators of inter-organ communication, particularly in the context of obesity and insulin resistance. In this study, we investigated the role of the adipocyte-expressed miRNA, miR-193a-5p, in maintaining metabolic homeostasis under both lean conditions and during diet-induced obesity. We found that miR-193a-5p was predominantly expressed in adipose tissue of mice and humans, and was inversely correlated with key metabolic disease traits, including body mass index (BMI), fat mass, insulin resistance, and serum triglyceride levels in humans. Additionally, genes positively associated with miR-193a-5p expression were involved in pathways related to fatty acid β-oxidation and mitochondrial respiration. Predicted targets of miR-193a-5p included repressors of thermogenesis and overexpression of miR-193a-5p in brown adipocytes enhanced thermogenic gene expression. Preliminary studies of a miR-193a-5p knockout mouse model are ongoing. Our findings establish a relationship between miR-193a-5p expression and metabolic health and provide further insights into tissue-specific expression patterns and potential functions of miR-193a-5p. These findings advance our understanding of miR-193a-5p as a potential regulator of thermogenesis and suggest its therapeutic relevance in treating obesity and its associated comorbidities.

Research Grant: CHOP Research Institute

Student Support: NIH grant T35OD010919-28 and the University of Pennsylvania School of Veterinary Medicine

16. DIFFERENCES IN EQUINE INTERVERTEBRAL DISC CELLULAR COMPOSITION ACROSS AGES.

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Neurological conditions, pain, and lameness are common in horses and typically originate from the neck. The non-traumatic and non-infectious causes of these conditions have been attributed to spinal cord compression through degenerative changes in the articular process joints (APJ), specifically osteoarthritis (OA), most commonly in the joint between C5-C6 and C6-C7. In humans, IVDD and APJ OA are closely related and often occur in tandem. While APJ OA of the equine caudal cervical spine has been shown to be a significant cause of neurological conditions, pain, and lameness, the IVD has not been well-studied in the past and there has been little consensus on the exact gross and microscopic morphology. In other mammals, the onset of intervertebral disc degeneration (IVDD) can be characterized by the change in NP cell population from large vacuolated notochordal cells (NC) to chondrocyte-like cells (CLC). The transcription factor brachyury is connected to notochord development and subsequent NCs. Using histological grading, characterization and brachyury immunohistochemistry we aim to describe the equine IVD across ages. We hypothesize that brachyury will be expressed in the youngest foals and that its expression will decrease with age and disc degeneration. These results will inform the strategy for appropriate clinical approaches to treat equine IVDD.

17. CHARACTERIZATION OF THE LIGAMENTUM MUCOSUM IN THE FELINE AND CANINE STIFLE.

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In humans, the ligamentum mucosum (LM) has been described as a ligamentous structure originating from the femoral intercondylar notch and inserting into the infrapatellar fat pad. Proposed clinical implications include knee stabilization, contribution to post-operative revascularization of adjacent structures, and causation of anterior knee pain if inflamed. Published reports of the LM are rare in dogs and, to our knowledge, none exist for cats. Because common veterinary gross anatomy texts omit the LM from their descriptive anatomy of the stifle, students sometimes mistake the LM for the cranial cruciate ligament when learning anatomy. Therefore, a description of the LM in the feline and canine stifle would serve as an important veterinary anatomy learning resource. The aim of this project was to characterize the LM in the cat and dog. Stifles were dissected from 62 cat hindlimbs (n=24 preserved, n=38 fresh) and 47 dog hindlimbs (n=9 preserved, n=38 fresh). The presence or absence of the LM was determined and descriptive characteristics recorded. Representative samples were processed for hematoxylin and eosin staining. Grossly, the LM was found bilaterally in 95.2% of cats and in 83.0% of canine limbs, appearing as an elastic, friable band of white-to-pink tissue tethering the infrapatellar fat pad to the femoral intercondylar notch. Histological samples revealed collagen fibrils, vascular structures and neural tissue. These data provide evidence of the LM in the cat and dog, and bolster currently available anatomic educational resources. The presence of the LM in the canine and feline stifle merits further investigation into its function and stability in health and disease states.

18. S. ANGINOSUS AND H. PYLORI SS1 CO-INFECTION PROMOTES GASTRIC PATHOLOGY IN GERM FREE INS-GAS MICE.

Isabella Lozano[1], Zeli Shen[2] , Zhongming Ge[2], Yan Feng[2], Magalie Boucher[2], and James G. Fox[2].

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Helicobacter pylori is remarkably prevalent in the human population, and it is a principal cause of gastric cancer. Previous studies have reported that *Streptococcus anginosus* was identified in high numbers in the gastric mucosa of gastric cancer patients. In SPF mice, *S. anginosus* caused gastritis, mucinous metaplasia, and dysplasia. Gastric inflammation was more pronounced in *H. pylori* and *S. anginosus* co-infected mice, and mice also had a relative risk of atrophic gastritis and subsequent progression to intestinal metaplasia and gastric cancer. Our study aims to further investigate the potential effect of *S. anginosus* co-infected with *H. pylori* SS1 in germ free insulin gastrin (INS-GAS) mice. In a pilot study we infected 18 mice with *S. anginosus*. We noted *S. anginosus* colonization in the stomach; infected mice had an increase in stomach pathology and Il-1β pro-inflammatory cytokine. In the current study, 80 mice were separated into 4 groups; uninfected control, *H. pylori* infected, *S. anginosus* infected, and co-infected. Bacterial colonization, stomach pathology scores, and pro-inflammatory cytokine gene expression were evaluated. 4 months post infection, *H. pylori* infected mice had a statistically significant increase in stomach to body weight ratios. *S. anginosus* colonized the stomach and intestines of the infected mice. There is no significant difference in colonization level of *H. pylori* or *S. anginosus* mono infection and co-infection group. Preliminary results indicate that the co-infected group have an increase in inflammation and hyperplasia/dysplasia, which appears to be more severe in male mice. This study demonstrates that *S. anginosus* may play a role in augmenting *H. pylori* induced gastric pathology.

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19. EFFECTS OF KDM1A AND SDHB KNOCKOUT ON DEVELOPMENT OF ADRENAL IPSC LINES.

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The KDM1A and SDHB genes are both highly conserved genes found in most mammals and are both essential parts of adrenal cell differentiation. KDM1A encodes for a histone demethylase protein which will serve to remove methyl groups on lysine residues found on histone proteins. Excessive histone methylation on site H3K4 (4th lysine residue on histone H3) could be a potential consequence of KDM1A dysfunction and contribute to increased likelihood of adrenal adenoma formation. Previous studies focused on KDM1A knockout procedures have identified its role in contributing to the development of adrenal hyperplasia, especially in relation with Cushing's syndrome. The SDHB gene encodes for a subunit of the succinate - dehydrogenase (SDH) complex that is involved in metabolic processes such as the Krebs Cycle and the electron transport chain (ETC). Knockout of the SDHB gene in conjunction with the NF1 gene has previously demonstrated increased likelihood of contributing to pheochromocytomas. The Sasaki Lab has developed the first human induced pluripotent stem cell (iPSC) - derived fetal organoid system in attempts to reveal some of the underlying mechanisms of adrenal development. These cells can mimic the natural development of human adrenal cortical cells that can serve as a base for our KDM1A KO experiment. Our intent was to make a KDM1A

and SDHB knockout line utilizing the Crispr-Cas9 system in human iPSCs. We utilized an all-in-one vector referred to as Px335-mCherry which contains the gRNA sequence and the Cas9 enzyme. After transfection to iPSCs, we selected the cells that expressed mCherry and confirmed indel mutations through Sanger sequencing for the *KDM1A KO* line. These mutant cell lines can be used to elucidate some of the mechanisms behind adrenocortical carcinomas and pheochromocytoma development in future projects.

Research Grant: NIH grant T35OD010919-28

Student Support: Sasaki Lab and the University of Pennsylvania School of Veterinary Medicine

20. QUANTIFICATION OF LAMELLAR EPITHELIAL CELL DEATH AND PROLIFERATION IN AN EXPERIMENTAL MODEL OF HYPERINSULINEMIA-ASSOCIATED LAMINITIS.

Megan McCathy, Andrew van Eps, and Jeaneen Kulp.

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Endocrinopathic laminitis is one of the most common forms of equine laminitis and is strongly associated with insulin dysregulation in horses with pituitary pars intermedia dysfunction (PPID) and equine metabolic syndrome (EMS). Experimental models have demonstrated that healthy horses subjected to prolonged hyperinsulinemia can develop laminitis within 48 hours; however, the precise mechanisms by which excess insulin affects lamellar tissue has not been quantified. Previous studies using a prolonged euglycemic hyperinsulinemic clamp (p-EHC) model have described lamellar epithelial stretching, increased mitotic activity, apoptotic basal cells at the dermal–epidermal junction, and marked basement membrane separation.

The primary objective of this study was to quantify epithelial cell death and proliferation during early and late stages of hyperinsulinemia-induced laminitis. Paraffin-embedded lamellar tissue samples were obtained from horses subjected to prolonged insulin infusion and harvested at 6, 12, 24, and 48 hours post-infusion, with healthy horses serving as controls. Tissue sections were analyzed using terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and caspase-3 immunohistochemistry to differentiate apoptotic from non-apoptotic cell death. Digital slide imaging and quantitative analysis were performed using QuPath software to assess the distribution and frequency of positive basal epithelial cells within the lamellae. We hypothesized that hyperinsulinemia is associated with increased apoptotic cell death in basal epithelial cells and increased cellular proliferation adjacent to keratinized lamellar axes during early disease development. The data aims to clarify early cellular events in laminitis and contribute to a more precise understanding of insulin-mediated lamellar pathology.

ORAL PRESENTATION

21. CONTROL OF YAP/TAZ SIGNALING ON MACROPHAGE FUNCTION DURING BONE HEALING.

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Bone tissue is unique in its ability to regenerate, restoring its original structure and function without scarring. Despite this, current treatments remain inefficient, costly, and limited. Taking advantage of biological repair processes—especially inflammatory and mechanical cues—may reveal new ways to enhance healing. Monocytes and pro-

inflammatory macrophages (MΦs) infiltrate the fracture site within 24–48 hours, coinciding with peak mechanical stimuli from interfragmentary motion. As healing advances, MΦs transition to anti-inflammatory phenotypes and influence chondro/osteogenesis and angiogenesis. Mechanical signals are transduced by the transcriptional regulators YAP and TAZ, which our group previously implicated in skeletal development and regeneration. While YAP/TAZ activity in osteoblasts is well-characterized, their role in MΦs remains poorly understood. Here, we explore how YAP/TAZ modulate MΦs mechanosensitivity and function during bone fracture repair. Using a LysM-Cre YAP/TAZ double-flox mouse model, we induced femoral osteotomies and stabilized fractures with either stiff or compliant fixators. Two weeks post-surgery, we assessed callus formation and mineralization via microCT and performed histological analyses to quantify MΦs infiltration, vascularization, and cell proliferation. No significant differences were observed in vessel density, MΦs numbers, or proliferative activity between groups. Preliminary data suggests that compliant fixation promoted greater interfragmentary motion, thus affecting bone healing (in WT mice- callus: 52.0 mm^3 compliant vs. 38.5 mm^3 rigid). Notably, YAP/TAZ deletion in MΦs under compliant fixation resulted in altered mechanosensation, thus diminished callus size but increased mineral density (callus: 52.0 mm^3 WT vs 33.1 mm^3 KO; bone density: 1.18 mm^3 WT vs 1.81 mm^3 KO). These findings suggest that YAP/TAZ are critical for MΦs-mediated mechanotransduction during fracture repair, and their dysregulation disrupts the mechanical responsiveness necessary for optimal healing.

22. GPS-TRACKING OF FREE-ROAMING DOGS AND HUMAN SPILLOVER RISK OF ECHINOCOCCUS GRANULOSUS IN HIGHLY ENDEMIC PERU.

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Cystic echinococcosis (CE), a neglected disease that results from infection with the larval stage of the *Echinococcus granulosus sensu lato (s.l.)* tapeworm, poses significant zoonotic risk to humans and is a persistent threat in developing agricultural communities around the world. While the prevalence of human CE in the central highlands of Peru has previously been estimated around 5–7%, true prevalence is likely higher given the protracted period of asymptomatic disease, reduced medical access of at-risk populations, increased contact between herders, livestock, and herding dogs, and poor understanding of local disease epidemiology. To better understand CE epidemiology in a highly endemic region of Peru, we studied the movement of free-roaming dogs in the community of Chanchayllo, Junin, Peru.

We performed copro-ELISA to identify positive dogs, tracked the ranging behavior and calculated home ranges of 19 owned, free-roaming dogs to understand the movement of the definitive host of *E. granulosus s.l.* on the landscape. Specifically, we investigated the spatial association between infected dog home ranges and proximity to their owners' houses and a local slaughterhouse. *Echinococcus granulosus s.l.* infection prevalence was alarmingly high in our canine population, with 85% positivity (binomial exact 95% CI: 62.1–96.8%). All dog home ranges overlapped with their owners' households, and notably, even negative dog households overlapped with nearby positive dog home ranges.

These data suggest that widespread environmental contamination of *E. granulosus s.l.* egg-containing feces may be a significant driver of locally elevated disease prevalence in human populations. We use our findings to understand the local disease ecology of CE in free roaming dogs, assess spillover risk, and guide future intervention strategies aimed at reducing human cases. Our findings suggest that existing strategies delivering anthelmintic drugs to individual households have the potential to reduce spillover of *E. granulosus s.l.*

23. LAMELLAR EPITHELIAL CELL PROLIFERATION AND DEATH IN THE OLIGOFRUCTOSE OVERLOAD MODEL OF SEPSIS RELATED LAMINITIS.

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Sepsis Related Laminitis (SRL) is a common secondary complication seen in hospitalized horses with systemic illnesses and resultant global inflammation due to endotoxemia caused by a variety of diseases. In cases of laminitis, common histopathology observed is stretching of the lamellar epithelial cells and failure of cell-cell adhesions and cell-basement membrane adhesions. Other histological changes that have been observed in previous SRL studies include keratinocyte cell death and proliferation. However, these studies were done using an unreliable carbohydrate overload model, producing a variety of results. The goal of this study was to characterize the cells in tissue samples collected from horses who were subjected to oligofructose overload as a model of sepsis related laminitis, a more reliable method of inducing SRL. Samples were collected from limbs 6, 12, 18, 24, and 54 hours post dosing and stained with TUNEL to mark cells undergoing non-specific cell death and a dual stain for Caspase-3 and Ki-67 that marked cells undergoing apoptosis and proliferative cells, respectively. We hypothesized that histological samples from the later time points would show increased numbers of proliferative cells and cells undergoing cell death, either non-specific or apoptotic. Gaining a better understanding of when cellular changes begin to occur will hopefully allow us to better describe the pathophysiology of SRL so we can better learn how to manage the disease and potentially develop more effective treatments.

Research Grant: Laminitis Research Fund

Student Support: NIH/Boehringer Ingelheim

24. EVALUATING THE ABILITY OF A RAPID, FIELD-DEPLOYABLE, ISOTHERMAL ASSAY TO SCREEN DECEASED AVIAN WILDLIFE FOR INFLUENZA A VIRUS.

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Highly pathogenic avian influenza (HPAI) encompasses a group of highly contagious avian influenza A viruses with zoonotic potential. Outbreaks have caused economic devastation in poultry globally and across the United States. HPAI is a public health concern both as a threat to national food security and its potential pathogenicity in humans. Waterfowl are reservoirs for avian influenza and facilitate the spread of the virus to other wildlife and domestic birds as they migrate. In 2021, HPAI strain H5N1 clade 2.3.4.4b was first introduced to North American flyways. H5N1 2.3.4.4b has demonstrated unique ability to cause high morbidity and mortality rates in a wide range of mammalian and avian species, as well as in its anseriforme reservoirs. For example, HPAI H5N1 killed over 5,000 snow geese in eastern Pennsylvania in January 2025. The ability to effectively and rapidly screen for influenza A during similar avian mortality events would improve the speed of response decisions, advisories to properties or institutions that house poultry, and sample submissions to diagnostic facilities while protecting the health and safety of wildlife officials. Here, we assessed the ability of the Biomeme Franklin portable thermocycler with an Influenza A matrix isothermal amplification assay

to detect the presence of influenza A virus in mucosal swabs obtained from known positive and negative birds. From the 76 samples tested, the Franklin demonstrated a sensitivity of 94.1% and a specificity of 100% with data obtained in 30 minutes. These results suggest potential for future field or point of care applications of this rapid isothermal technology.

Research Grant: RK Mellon Foundation

Student Support: NIH/Boehringer Ingelheim

25. GENETIC MODIFICATION TO rVSV-HRTV VIRUS IMPROVES EFFICACY AS VACCINE CANDIDATE.

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Heartland virus (HRTV) is an emerging tick-borne virus in the *Bunyaviracetes* class and *Bandavirus* genus. Although there are relatively few reported cases of HRTV infection, the case fatality rate is high, and surveillance studies in wildlife have shown significant viral circulation. For this reason, HRTV is considered to have pandemic potential and has been classified as a priority pathogen by the National Institute of Allergy and Infectious Diseases (NIAID). Despite this threat, no studies evaluating HRTV vaccines have been published.

One vaccine candidate that shows early promise for HRTV is the recombinant vesicular stomatitis virus (rVSV) vaccine, which can be engineered to express foreign glycoproteins on virions. rVSV vaccines developed for other viruses, including members of the same genus, induce strong immune responses and are protective against lethal challenge. However, rVSV-HRTV is attenuated in cell culture, which may be due to incompatibility between the assembly sites of HRTV (the Golgi and ERGIC) and VSV (the plasma membrane).

We have identified a mutation in a non-canonical COPI binding motif found in the cytoplasmic tail of HRTV glycoproteins, which we call K1074A. Our data demonstrates that mutation of this COPI binding motif results in increased surface expression of bandavirus glycoproteins, which may allow for more efficient incorporation onto VSV particles. The K1074A mutation dramatically increases the efficiency of rVSV rescue and improves viral replication kinetics compared to rVSV with the WT HRTV glycoprotein, allowing increased efficiency of vaccine production. Importantly, the mutation also positively impacts replication *in vivo*, and vaccination with rVSV-HRTV K1074A results in improved induction of neutralizing antibody responses in immunocompetent C57BL/6 mice. Studies are underway to evaluate the protective efficacy of serum transfer from C57BL/6 mice vaccinated with rVSV-HRTV K1074A and determine whether neutralizing antibodies are sufficient for protection of severely immunodeficient AG129 mice from lethal HRTV challenge.

26. EXAMINATION OF THE CHONDROPROTECTIVE EFFECTS OF IFN-γ PRIMED EXTRACELLULAR VESICLES PRODUCED BY EQUINE BONE MARROW-DERIVED MSCs.

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Osteoarthritis (OA) is a chronic, progressive disease. Current therapies primarily address pain and do not target the underlying disease process. Bone marrow–derived mesenchymal stem cells (BM-MSCs) have demonstrated immunomodulatory potential, but clinical use is limited by culture time and immune responses. As an alternative, the BM-MSC secretome, particularly extracellular vesicles (EVs), has been investigated as a cell-free therapy. Priming BM-MSCs with interferon-gamma (IFN-γ) has been shown to enhance their immunomodulatory effects. We hypothesized that EVs derived from IFN-γ–primed equine BM-MSCs would exhibit enhanced anti-inflammatory and chondroprotective properties compared to unprimed EVs in an *in vitro* OA model. Equine BM-MSCs were cultured with or without IFN-γ, and EVs were isolated by stepwise ultracentrifugation. EV presence and concentration were confirmed using Western blot and nanoparticle tracking analysis. EVs were applied to chondrocytes stimulated with IL-1β to mimic OA conditions *in vitro*. Markers of inflammation and matrix degradation were assessed using qRT-PCR and fluorescent multiplex immunoassay. A scratch assay was performed to evaluate chondrocyte proliferation. Fluorescent multiplex immunoassay revealed a significant decrease in IL-1β concentration in stimulated cultures treated with primed and unprimed EVs compared to stimulated controls. qRT-PCR revealed significantly increased expression of IL-6 and ADAMTS4 in stimulated chondrocytes treated with primed EVs compared to stimulated controls. MMP13 expression was significantly increased in stimulated chondrocytes treated with unprimed EVs compared to stimulated controls. There were no significant differences between treatment groups in the scratch assay. EV treatment decreased synthesis of the inflammatory cytokine IL-1β as reflected in supernatant concentrations, however, gene expression of IL-1β was not significantly different which may reflect the impact of miRNA-rich EVs on translation and protein synthesis. These results suggest a complex interplay of cell signaling. Future studies are needed to further characterize the pro- and anti-inflammatory nature of IFN-γ-primed EVs prior to therapeutic use.

Research Grant: Raymond Firestone Trust

Student Support: NIH/Boehringer Ingelheim

27. INVESTIGATING THE EFFECTS OF THE p38 INHIBITOR RALIMETINIB ON CANINE CAR T CELLS.

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Introduction: Chimeric antigen receptor (CAR) T cells are T cells that are genetically modified to target antigens expressed by cancer cells. CAR T therapy has revolutionized the treatment of hematologic malignancies but has been less successful against solid tumors. The intrinsic fitness of T cells used to make a CAR T product can influence anti-tumor activity, and this has motivated researchers to investigate techniques to enhance CAR T activity against solid tumors. Previous studies have revealed that inhibition of p38 kinase promotes memory phenotypes and enhances the cytotoxicity of murine and human CAR T cells, thus improving anti-tumor activity in multiple tumor models. The aim of this study was to examine the effects of the p38 inhibitor, ralimetinib, in canine CAR T cells directed against the aggressive canine solid tumor histiocytic sarcoma (HS).

Methods: To determine if ralimetinib has on-target activity in canine cells, we have cryopreserved supernatants from peripheral blood monocytes (PBMCs) that have been stimulated in the presence or absence of ralimetinib alongside unstimulated controls. ELISA will be used to quantify TNFα secretion as a surrogate of p38 inhibition, as ralimetinib decreases TNFα secretion in other species. In ongoing work, canine CAR T cells directed against HS are being expanded in the presence or absence of ralimetinib to determine the impacts of p38 inhibition on canine CAR T cells. Using flow cytometry, we are interrogating the memory status of canine CAR T cells by quantifying CD62L expression. Finally, we are assessing the cytotoxicity of CAR T cells against canine DH82 HS cells.

Conclusions: These data will determine if p38 inhibitor ralimetinib can be used to improve the preclinical activity of canine CAR T cells.

Research Grant: NIH K08 CA2526519

Student Support: NIH T35 OD010919-28 and the University of Pennsylvania School of Veterinary Medicine

28. GEOGRAPHIC DISTRIBUTION OF THE EMERGING ZOONOTIC EYEWORM THELAZIA CALLIPAEDA IN THE NORTHEAST USA.

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Thelaziosis is an emerging zoonotic disease caused by spirurid nematodes of the genus *Thelazia*. *Thelazia callipaeda* is the main agent of ocular thelaziosis in mammals in Asia and Europe, and its prevalence has been increasing globally over the past decade. The first autochthonous case in the United States was reported in 2020 in a domestic dog in New York. This eyeworm is transmitted by the male secretophagous fruit fly, *Phortica variegata*, which occasionally feeds on mammalian lachrymal secretions. The aim of this study was to investigate host susceptibility to *T. callipaeda*, identify potential environmental and host determinants influencing transmission, and to provide insights into the epidemiology of *T. callipaeda* in companion animals in the USA. A total of 36 samples were obtained from multiple locations in PA, NJ, CT, and NY. When available, information about the host was recorded, including geographic location, clinical signs, breed, age, sex, and travel and medical history. Adult specimens were preserved in 70% ethanol and subjected to morphological and molecular analysis. Genomic DNA was extracted from a fragment of the middle body of adult female worms. Molecular analysis was performed by targeting a fragment of the mitochondrial cytochrome c-oxidase subunit 1 (*cox*1). Phylogenetic analysis was performed using MEGA X 11, comparing sequences to those available on GenBank. Case distribution was mapped using ArcGIS pro, overlaid with vector-relevant environmental factors. These data illustrate the spread of *T. callipaeda* in the northeast area of the United States. Considering the of emergence *T. callipaeda* in non-endemic areas, it is necessary to identify parasite dynamics, potential reservoirs, and host-related factors that contribute to the spread of the disease in the USA.

Research Grant: 2025 McCabe Fund Pilot Award

Student Support: NIH/Boehringer Ingelheim

29. THE PATHOLOGY OF EASTERN EQUINE ENCEPHALITIS IN FREE-RANGING AVIFAUNA IN THE EASTERN UNITED STATES.

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Eastern equine encephalitis virus (EEEV) is a mosquito-borne alphavirus that can cause neurological disease in avian and mammalian species. While passerines are considered subclinical virus-amplifying hosts, disease manifestations in other wild birds remain less well documented. To investigate the spectrum of EEEV-induced lesions in wild avifauna, we reviewed cases submitted to wildlife diagnostic laboratories confirmed as EEEV-positive by virus isolation and/or PCR. Identified cases comprise wild turkeys (WITU; n=4) and raptors (n=6) including the barn owl (ABOW), great horned owl (GHOW), Cooper's hawk (COHA), red-shouldered hawk (RSHA), osprey (OSPR), and bald eagle (BAEA). Three WITU showed lymphoplasmacytic meningoencephalitis, while one had suspected brain inflammation based on perivascular cuffing despite autolysis. Visceral lesions were also common in WITU and included interstitial nephritis (n=2), myocarditis (n=1), and splenic necrosis (n=1), while two also had avian pox. All four WITU had at least one extraneural (dermal or visceral), EEEV-induced lesion. In contrast, raptors were more likely to show isolated CNS involvement without visceral lesions. Classic EEEV-associated meningoencephalitis was observed in ABOW, COHA, and BAEA, and included lymphoplasmacytic and heterophilic inflammation, neuronal necrosis, and gliosis. RSHA had myocarditis without brain lesions. EEEV was detected in OSPR and GHOW (by PCR and virus isolation) but tissue autolysis and limited availability precluded histopathology. These findings highlight species-specific variation in lesion patterns, with WITU showing more systemic involvement and raptors exhibiting primarily neurotropic disease. Recognizing key histologic lesion patterns across differing avian species may improve diagnostic accuracy and thus strengthen EEEV surveillance efforts in free-ranging avian populations.

30. USING ENHANCER ADENO-ASSOCIATED VIRUSES TO DISSECT PRE-OPTIC AREA NEURONS THAT REGULATE BODY TEMPERATURE.

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To survive extended periods of fasting, animals undergo dramatic metabolic, homeostatic, and activity changes known as torpor and hibernation. Most notably, these states involve a marked decrease in body temperature with a concomitant drop in metabolic rate. The preoptic area of the hypothalamus (POA) has been extensively studied for its role in maintaining homeostatic functions, including body temperature. However, the specific neuronal populations involved in thermoregulation are not fully known. Moreover, it remains unclear whether the neural circuits that control torpor in mice are conserved in other species that exhibit torpor and/or hibernation. The use of transgenic lines is a powerful tool in mouse research, but this approach is often impractical or unavailable in other species. To address these challenges, we identified subsets of neuronal populations in the POA that may drive torpor and developed enhancer adeno-associated viruses (AAVs) to target such neuronal populations specifically. Here, we demonstrate it is possible to achieve a high degree of targeting specificity with this strategy. We further show proof of concept that enhancer-driven AAVs can generate sufficient expression to elicit functional changes in body temperature upon stimulation. These experiments establish a platform for investigating conserved torpor-regulating circuits in non-model species.

Research Grant: NIH DP2DK136123

Student Support: Summer fellowship funding from NIH T35 OD033655

ORAL PRESENTATION

31. INVESTIGATING UNIQUE INTESTINAL EPITHELIAL CELL STATES THAT ARISE DURING CHRONIC INFLAMMATION.

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In patients with inflammatory bowel disease (IBD), dysregulated immune response and impaired mucosal healing lead to chronic inflammation. Our lab has identified a unique cell state, which we termed the inflammatory secretory progenitor (ISP), in the intestinal epithelium of pediatric and adult patients with Crohn's disease. The ISP gene signature is found in OLFM4^{low}REG1A^{high} secretory progenitors that express an inflammatory profile of immune-related and antimicrobial peptides, and antigen presentation proteins (e.g. MHC II). The functional consequences of the ISP cell state and its role in IBD pathogenesis have yet to be explored. We posit that cells in an ISP state modulate epithelial responses to injury and sustained inflammation that may impair epithelial regeneration and exacerbate disease pathogenesis. Importantly, the signaling pathways involved in ISP development are unclear. Recently, we utilized double positive HLADR^{+}HLADP^{+} cells (MHC II isotypes) as markers for the ISP cell state and induced this cell state with acute treatment in patient-derived colonoids using a previously validated inflammatory cocktail (TNFα, IL1β, IL6, Flagellin). ISP-like induction was much higher in colonoids derived from patients with Crohn's following acute cocktail treatment, with little induction in control lines. We hypothesize that chronic inflammatory treatment is required in non-disease colonoids for ISP cell state induction. To dissect the induction paradigms required to elicit an ISP cell state, we developed an *in vitro* system to test acute vs chronic inflammatory stimulation in non-disease colonoids. We then evaluated self-renewal and proliferative capacity as well as necessity of specific cocktail components in ISP-like cells derived from non-disease colonoids. Preliminary results demonstrate after chronic treatment, there is robust upregulation of ISP markers in non-disease colonoids with more than 25% of cells expressing HLADR/HLADP as we saw in Crohn's colonoids after acute treatment. To characterize the progenitor-like nature of the ISP-like cell state *in vitro*, we sorted HLADR^{+}HLADP^{+} cells and examined their ability to form colonoids. Double positive HLADR^{+}HLADP^{+} colonoids grew similarly to colonoids derived from HLADR^{-}HLADP^{-} cells, supporting the self-renewal and proliferative capacity of these cells. Finally, initial results suggest that TNFα in the cocktail treatment is the primary driver of double positive induction after both chronic and acute treatment. Our studies demonstrate that chronic inflammatory treatment induces an ISP-like cell state in non-disease colonoids similar to that seen in Crohn's disease colonoids, with TNFα identified as a primary driver. Ongoing studies will evaluate whether ISP-like cells have impaired self-renewal capacity compared to non-inflammatory progenitor cells and define mechanisms underlying TNFα-mediated ISP emergence.

Support and Funding Information: University of Pennsylvania School of Veterinary Medicine; Institute for Infectious & Zoonotic Diseases Martin and Pamela Winter Infectious Disease Pre-Doctoral Fellowship

32. INVESTIGATION OF EPIGENETIC FEATURES OF THE X-CHROMOSOME IN LYMPHOCYTES FROM SCLERODERMA PATIENTS.

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Systemic Sclerosis (SSc) is an autoimmune fibrotic disease that preferentially affects women. The molecular basis of this disease remains unknown, but epigenetic dysregulation of the inactive X chromosome (Xi) may contribute. In past studies, circulating lymphocytes from patients with systemic lupus, another female-biased autoimmune disease, exhibited reduced localization of repressive epigenetic marks, including XIST RNA and H3K27me3, at the Xi, in association with the overexpression of pro-inflammatory X-linked genes. T cells have a known role in SSc pathogenesis, thus we hypothesized that T cell subsets from females with SSc may also exhibit the same epigenetic dysregulation at the Xi. Naïve and effector/memory CD4+ and CD8+ T cells from female SSc patients (n=25) and healthy female controls (n=25) were sorted via flow cytometry and cytospun onto glass slides in preparation for sequential XIST RNA FISH and H3K27me3 IF analysis. XIST RNA signals were classified using an ordinal scale based on localization and brightness of XIST puncta within the nuclei of cells. H3K27me3 signals were dichotomously categorized as present or absent depending on the presence of a focal nuclear signal. We found that effector/memory, but not naïve, T cells from females with SSc exhibit more dispersed XIST RNA patterns, in conjunction with lower proportions of nuclei with H3K27me3 foci, compared to those from healthy females, suggesting that XCI is impaired in T cells from patients with SSc. These data provide the first evidence of impaired XCI in T cells as a mechanism of female-biased disease in SSc, thus encouraging future studies to define the transcriptional and epigenetic landscape of the Xi in females with this disease.

33. IN-CAGE SMOOTHIE-BASED REWARD SYSTEM FOR BEHAVIORAL RESEARCH IN NON-HUMAN PRIMATES.

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Non-human primates are the ideal animal model to support behavioral research and cognitive training. A custom-built in-cage reward system was designed to dispense a smoothie-based reward during voluntary engagement of cognitive tasks. By allowing animals to remain in their home cages during task engagement, we reduce stress and encourage more naturalistic behavior, ultimately improving both the ethical standards and the quality of the research. The primary goal of this system is to prioritize animal welfare while maintaining high scientific standards. Through these improvements, we aim to build a more ethical and effective model for translational neuroscience research. The developed system is centered around a peristaltic pump controlled by a Raspberry Pi 4B, which receives wireless reward triggers from behavioral software, NIHM MonkeyLogic, running on a tablet. Successful task completion relays a signal to the pump, which activates and dispenses a small, calibrated volume of smoothie through a metal rod accessible within the animal's home cage. Smoothie mixtures offer a palatable and nutritionally balanced approach that has shown an increase in motivation, particularly among female animals, fostering more consistent and inclusive participation. The smoothie-based reward provides the landscape to adjust taste profiles to suit individual animal health status and preference. Overall, this system represents a major refinement in the way behavioral research is conducted with non-human

primates. It aligns with the ethical principles of refinement and reduction, offering a more humane and scientifically robust methodology. It also enhances gender inclusivity, supports long-term health, and provides a scalable framework for future innovations in autonomous training and welfare monitoring.

Student Support: Boehringer-Ingelheim and the University of Pennsylvania School of Veterinary Medicine

ORAL PRESENTATION

34. ASSESSMENT OF THE EFFECT OF PROBIOTICS ON THE CALF MICROBIOME THROUGH THE PREWEANING PERIOD.

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Microbial homeostasis during the preweaning period in neonatal calves is linked to improved weight gain and disease resistance, while dysbiosis increases susceptibility to pathogens and reduces long-term health and productivity. Early life colonizing bacteria such as *Faecalibacterium* spp. (FP), *Blautia* spp. (BS), and *Bacteroides* spp. (BT), have been shown to improve colonic epithelial homeostasis and exert anti-inflammatory effects via butyrate production and substrate cross-feeding. Although these taxa form a beneficial consortium, their synergies and impact on the microbiota during the preweaning period remain unclear. The objective of this study is to elucidate how FP, BS, and BT metabolically interact with the calf microbiome during early (1-4 weeks) and later (5-8 weeks) phases of the preweaning period. Using Holstein calf feces, the gut microbial communities were modeled in the *in vitro* ANKOM system. The treatments included inoculation with FP and BS, FP and BT, FP, BS, and BT, cultural media only, or a negative control of feces only (n=3). The experiment was run twice, with each run incubated for 24h, where pH, redox and fatty acid composition were assessed at 0 and 24h and gas (CO_2, H_2, and CH_4) concentrations were measured at 12 and 24 hours via gas chromatography. Preliminary results showed that total gas production increased over time, indicating fermentation rates were maintained. However, H_2 and CH_4 production were consistently reduced in 1–4-week microbiomes treated with FP+BS and FP+BS+BT, indicating a shift in fermentation patterns. These results suggest the potential of probiotic therapies during the preweaning period in beneficially modulating gut microbiota and improving animal health and development.

Research Grant: NIH grant T35OD010919-28 and the University of Pennsylvania School of Veterinary Medicine

35. LEVERAGING COMPARATIVE ONCOGENOMICS TO ADVANCE AN UNDERSTANDING OF COPY-NUMBER ALTERATIONS IN CANCER.

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Copy Number Alterations (CNAs), mutational events characterized by gains or losses of chromosomal material, are a hallmark of cancer genomes, contributing to tumor initiation, progression, and response to therapy (Beroukhim et al., 2010). While the role of CNAs in cancer development is well-appreciated, the exact genetics and downstream biology that is consequent to these events remains muddy. Recent comparative oncogenomic studies have proven spontaneously arising tumors in dogs valuable models for the study of cancer. For example, dog cancers share

significant similarities to human cancer in molecular and pathologic features (Gardner et al., 2016). However, it is currently unknown to what extent, if any, their shared CNAs overlap. Here, this study aims to utilize recently developed methodologies for high-throughput oncogenomic sequencing to analyze CNA profiles in diverse tumor types—osteosarcoma, lymphoma, melanoma, mast cell tumors, and hemangiosarcoma—across both canine and human cohorts. Through employing high-throughput, high-resolution genomic technologies and cross-species bioinformatic analyses, we identified conserved and syntenic CNAs that may drive tumor biology. We argued that studying genomic similarities in cancers across species will not only enhance our understanding of genetics and the biology of cancer, but will also facilitate further development in precision medicine and targeted therapies benefitting both veterinary and human oncology.

36. CONTROL OF LYMPH NODE HIGH ENDOTHELIAL CELL FUNCTION BY IKKα.

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Lymphocyte recirculation through secondary lymphoid organs maintains effective immunosurveillance. To enter lymph nodes (LNs) lymphocytes migrate across specialized post-capillary venules named high endothelial venules (HEVs) lined by cuboidal endothelial cells (ECs) that express specific chemokines and adhesion molecules. Intriguingly, HEVs are surrounded by perivascular reticular cells (PRCs) and fibroblastic reticular cell conduits, which deliver small molecules from draining lymph directly to HEVs. Maintenance of HEVs requires non-canonical NF-κB activation by the upstream IκB Kinase (IKK)-α; however, how EC-intrinsic IKKα controls the phenotype and function of HECs has not been determined. To investigate this, the May lab created a constitutive knockout mouse model ($Ikk\alpha^{Vec}$) and found that loss of IKKα in ECs during embryonic development disrupts HEV function and potentially compromises the perivascular sheath. To determine how induced loss of IKKα in ECs in adult mice affects HEV function we developed a new tamoxifen (TX) inducible endothelial cell- knockout mouse model ($Ikk\alpha^{Cdh5\text{-}ERT2}$). Following TX treatment of $Ikk\alpha^{Cdh5\text{-}ERT2}$ mice we performed detailed immunofluorescence microscopic analysis of peripheral LNs, and our findings indicate that B cell populations are diminished and HEV morphology is disrupted. Moreover, structural integrity of the perivascular sheath is impacted by IKKα loss, and our ongoing experiments will determine if this affects the function of the conduit system. Taken together our new data suggests that IKKα signaling in HECs maintains the HEV perivascular sheath, revealing an entirely novel mechanism of IKKα-dependent crosstalk from HEVs to the nearby stromal cell network.

Research Grant: NIH Grants T35OD010919-28, R21AI173679

Student Support: Boehringer Ingelheim Summer Scholar's Award

37. PHARMACOLOGICAL MODULATION OF G-QUADRUPLEXES IN ACCELERATING MUSCLE REPAIR IN DUCHENNE MUSCULAR DYSTROPHY.

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Duchenne Muscular Dystrophy (DMD) is a fatal X-linked degenerative muscle chronic injury disease and among the most lethal inherited disorders in children. While progress has been made over the last decade with respect to

potential therapies for DMD, there is still no effective treatment. Although DMD is initiated and driven by dystrophin deficiency; the unrelenting, repetitive damage elicits a constant need for regeneration which is linked to dysfunction and impaired myogenesis. Muscle Stem Cells (MuSCs) play a critical role in this regenerative process. G-quadruplex DNA structures (G4s) are abundant in stem cells and have been found to be key structures related to cellular fate and differentiation. However, the role of G4 structures in MuSC regulation has never been reported. We hypothesized that G4 architectures in MuSCs are dynamically regulated during muscle regeneration and controlling their regenerative capacity. In this study, we administrated TMPyP4, a known G4 stabilizer, into mice after muscle injury to investigate the impact of G4 modulation on muscle remodeling and repair. We tested doses of 5, 10, and 20 mg/kg given 1- and 4-days post-injury to assess their effect on the regenerative capacity, as well as potential toxicity. It does not appear that the TMPyP4 drug has a beneficial impact on muscle regeneration of WT mice. Thus, we are not sure whether this compound can improve muscle repair of dystrophic mice, which can be proposed as a future direction. We can at least confirm that this compound is non-toxic in wildtype mice.

Research Grant: NIH/NIAMS (R01HL146662); Penn Discretionary Funds

Student Support: NIH/Boehringer Ingelheim

38. INCREASED TOTAL DURATION OF PENILE PROLAPSE DURING TRAZODONE TREATMENT IN HORSES.

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Trazodone is an anxiolytic with mild sedative properties. In spite of little research on safety, it is now widely used off label in veterinary medicine, including horses. Due to the nature of their husbandry conditions, stallions are one segment of the domestic equine population for which anxiolytics are commonly considered. When considering any medication in a breeding stallion, safety and potential adverse effects on breeding behavior and/or fertility are especially important. Accordingly, we are interested in the efficacy and safety of trazodone use in stallions.

One of the reported adverse side-effects of trazodone treatment in humans is priapism (persistent penile erection). Because of the dependent nature of the equine prolapsed penis, priapism typically progresses rapidly to paraphimosis (inability to retract the penis). Even when the paraphimosis is found early and can be effectively reduced, within only a couple hours of prolapse, fibrosis of the delicate erectile tissues can lead to permanent penile paralysis and inability to achieve erection sufficient for breeding or semen collection.

In a within-subjects repeated-measures design we have evaluated penile prolapse in 5 geldings during treatment with each of two doses of trazodone and placebo (using archived video from Hobbs et al, 2023). The mean (sd) percentage of time of penile prolapse was 1.3 (0.76) during control, 2.4 (2.2) during low dose treatment, and 4.2 (1.5) during medium dose treatment, with the medium dose significantly greater than control (dependent t-test, $P < 0.005$). Of note, for one of the geldings, penile prolapse time was 5 times greater during trazodone treatment than during control treatment, both with low and medium doses.

Work is currently underway to similarly evaluate effects of trazodone treatment on penile prolapse in stallions. Until these and other potential side-effects are better understood in horses, trazodone treatment of male horses should be carefully considered and monitored.

39. IMAGING MASS CYTOMETRY REVEALS A DYNAMIC SYNOVIAL CELLULAR LANDSCAPE IN CANINE CRUCIATE LIGAMENT DISEASE.

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Disease of the canine cranial cruciate ligament (CCL), the functional equivalent of the human anterior cruciate ligament (ACL), results in synovial inflammation and fibrosis that drive progressive joint degeneration and pain in CCL disease (CCLD). A clinical case review showed a correlation between symptom duration and arthroscopic inflammation scores. Synovial biopsies from CCLD dogs also demonstrated increased inflammation and fibrosis, greater stiffness, and inflammatory or immune cell activation, though prior studies did not evaluate cellular phenotypes or spatial organization in the diseased synovial microenvironment. Imaging mass cytometry (IMC) studies in mouse synovium have shown dynamic post-injury changes, including fibroblast activation and immune cell infiltration. Here, we used IMC to evaluate cellular changes in naturally occurring diseased CCL canine synovium, focusing on fibrotic, inflammatory or immune, and vascular markers, representing the first application of IMC to canine musculoskeletal tissue in this context. We hypothesized that advanced CCLD would show increased cell populations expressing these markers. Synovial samples were analyzed using IMC and immunofluorescence to phenotype fibrotic, inflammatory or immune, and vascular markers while preserving tissue architecture, with biomarkers selected from Hyperion-compatible human IMC panels based on cross-reactivity with canine targets to ensure reliable profiling. Histopathologic evaluation guided region-of-interest selection for IMC. Histology demonstrated synovial lining hyperplasia and expansion of the sub-synovial stroma with collagen deposition, more pronounced in CCLD patients with higher inflammation and fibrosis scores, confirming substantial tissue remodeling. IMC revealed distinct immune and stromal populations defined by unique protein expression patterns, with CCLD samples showing greater numbers of cells per region of interest and shifts in fibroblast and macrophage populations compared to controls. Correlation of IMC data with histopathologic scoring identified associations between stromal and inflammatory populations and synovial disease severity. These results support the hypothesis that macrophage-rich microenvironments, potentially localized near vascular and fibroblast populations, increase within inflamed synovium and scale with disease burden, aligning with findings describing the pro-inflammatory synovial landscape after human ACL injury and supporting the translational relevance of canine synovium as a model for human pathology and therapeutic evaluation.

40. UNCOVERING VIRAL PATHOGENESIS OF OROPOUCHE VIRUS: REPRODUCTIVE TRACT VIRAL KINETICS.

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Oropouche virus (OROV) is a re-emerging arbovirus and the current cause of outbreaks in several Latin American countries, as well as imported cases in North America. Clinical and epidemiological evidence suggest that OROV has the capacity to transmit vertically to the developing fetus, and there may be implications for risk of sexual transmission. This virus is transmitted primarily by Culicoides paraensis, a species of biting midge widely distributed throughout the Americas. Infected patients typically develop Oropouche fever, a viral illness typically characterized by flu-like symptoms. Oropouche fever may carry the risk of more serious and life-threatening complications, especially in

gestational patients. There is currently no specific treatment or vaccination available for OROV. Given the re-emergence and aforementioned risks of OROV, there is an urgent need to investigate the transmission and pathogenesis in a mouse model. Currently, there are very limited findings from immunocompetent mouse models for OROV infection. Our project has set out to develop and study OROV pathogenesis in the reproductive tract in an immunocompetent mouse infection model. We found wildtype (WT) male mice administered anti-interferon 1 receptor (anti-IFNAR1) antibodies prior to inoculation with OROV sustained high viral loads in all tested systemic tissues. Additionally, we found viral RNA present in both the male and female reproductive tract. Viral loads were significantly greater in anti-IFNAR1 treated mice than those treated with the isotype control antibodies in all tissues. This model of OROV pathogenesis and viral kinetics will be valuable in further assessing the risk and immunologic determinants of OROV sexual transmission and reproductive pathology. Further, our work will serve as a framework to further investigate the potential implications on sexual and reproductive health, including gestation and fetal development, sperm health and viability, and sexual transmission risk.

41. INVESTIGATING THE DIFFERENCE IN POST MYOCARDIAL INFARCTION REMODELING IN REPERFUSED VS NON REPERFUSED PATHOLOGIES.

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The incidence of sudden cardiac death (SCD) in the United States is estimated to occur as high as 450,000 cases annually and corresponds to 7-18% of all deaths. SCD is frequently attributed to circulatory collapse following the initiation of lethal ventricular arrythmias, such as ventricular tachycardia (VT). The patho-physiology of scar related VT includes structural and electrical remodeling that comprises areas of fibrosis and reduced, lateralized gap junctions. The result of slow, non-uniform anisotropic conduction promotes reentry and the foundation for lethal VT. Furthermore, the post-infarct substrate and associated characteristics in reperfused (IR) vs chronic total occluded (CTO) myocardial infarctions have not been well characterized. The objective of this study was to compare the structural and electrophysiological changes that occur due to reperfusion. Previous observation has led to the hypothesis that reperfusion would lead to a decrease in fibrosis density and an increase in scar heterogeneity. To further characterize this, two clinically relevant porcine models of post-infarction VT was created in 14 Yorkshire swine and separated into CTO groups (n=7) and IR groups (n=7). High resolution LV mapping studies and *in vivo* cardiac MRI were performed to measure LV myocardial volume, ejection fraction, and LGE (scar volume) across study groups. Masson's Trichrome and immunohistochemistry histological staining were performed to assess degree of fibrosis and connexin percentages. The major findings include the following: (1) creation of a chronic infarct results in significantly less heterogeneity and smaller areas of patchy arrhythmogenic substrate (2) chronic infarctions have significantly reduced connexins within scar area than reperfused models (3) chronic infarctions have significantly more fibrosis within core scar, allowing the substrate to conduct proarrhythmic slow conduction pathways. The data promotes the further investigation into various therapeutic techniques for patients post infarction.

Student Support: NIH/Boehringer Ingelheim

42. CHRONIC VASH INHIBITION IMPROVES DIASTOLIC FUNCTION IN A RAT MODEL OF HEART FAILURE WITH PRESERVED EJECTION FRACTION.

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Heart failure with preserved ejection fraction (HFpEF) is a clinical syndrome that comprises the majority of heart failure in human patients. Cardiac manifestations of HFpEF include diastolic dysfunction and left ventricular hypertrophy, but the molecular underpinnings remain to be elucidated. One change that has been observed in failing hearts is an increase in α-tubulin detyrosination, a post-translational modification that stabilizes polymerized microtubules and impairs myocardial relaxation. Detyrosination is mediated by vasohibins (VASH1/2), and this pathway represents a possible avenue to intercept the pathological changes that underlie diastolic dysfunction in HFpEF. A small molecule inhibitor of VASH (VASHi) has been shown to improve myocardial relaxation in the ZSF1 obese rat model of HFpEF after acute dosing. In this work, we aimed to assess the effects of longer-term administration of VASHi in ZSF1 rats. These rats, alongside a control group, were orally dosed daily with VASHi (200 mg/kg) for 8 weeks. Echocardiography was performed at regular intervals throughout the study and invasive hemodynamics was conducted at the conclusion. Detyrosination levels were also measured at the endpoint. ZSF1 obese rats dosed with VASHi had normalized detyrosination levels compared to their vehicle-dosed counterparts and had corresponding improvements in left ventricular end-diastolic pressure and relaxation time. Additionally, VASHi-treatment attenuated pathologic cardiac hypertrophy in male ZSF1 obese rats vs. vehicle-treated male controls, but the antihypertrophic effect was not observed in VASHi-treated females, suggesting an improvement in hypertrophy in the males. Of note, VASHi treatment did not lower body weight or blood pressure in ZSF1-obese rats. In all, these results support the microtubule network as a therapeutic target for HFpEF and the use of VASHi as a therapy, which could have implications for the treatment of heart failure in human and veterinary patients.

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Student Support: NIH T32

ORAL PRESENTATION

43. INVESTIGATING CHANGES TO THE CANINE GUT MICROBIOME IN THE SHELTER SETTING.

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Evidence that the gut microbiome impacts the health and behavior of humans and animals continues to grow. Existing canine studies have found similar results when comparing behavioral profiles to differences in gut microbiome composition, implicating the potential use of the microbiome as a biomarker for stress. In the animal shelter setting, a dog experiencing a prolonged stay may develop chronic stress, which can manifest as behaviors that reduce desirability for adoption. While several studies have found associations between dog behavior and microbiome composition, there have not been any studies investigating whether an individual's microbiome changes after entering the shelter setting. The aim of this study was to determine whether the composition of the gut microbiome changes significantly as a dog resides in the shelter. Comparisons between microbiome composition relative to shelter location and reason for admission were also explored. From October 2023 to August 2024, fecal samples were collected from a total of 37 dogs residing in three shelters in the Philadelphia area. Initial fecal samples were collected 0-48 hours after shelter admittance. Subsequent samples were collected at 7-9 days, 21-23 days, and 28-30 days post admittance. Microbial DNA were processed using shotgun metagenomic sequencing, and relative abundances of bacterial taxa were compared for individual dogs at each timepoint. PERMANOVA with Bray-Curtis analysis showed a significant difference ($p<0.05$) in relative gene abundances between samples from different timepoints for individual dogs. Differences in relative gene abundances and shelter location and reason for intake were also statistically significant. Factors other than stress likely influence the composition of the gut microbiome in sheltered dogs, limiting its current utility as a stress biomarker. However, the data collected in this study provide foundational insight on the impact sheltering may have on the gut microbiome.

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