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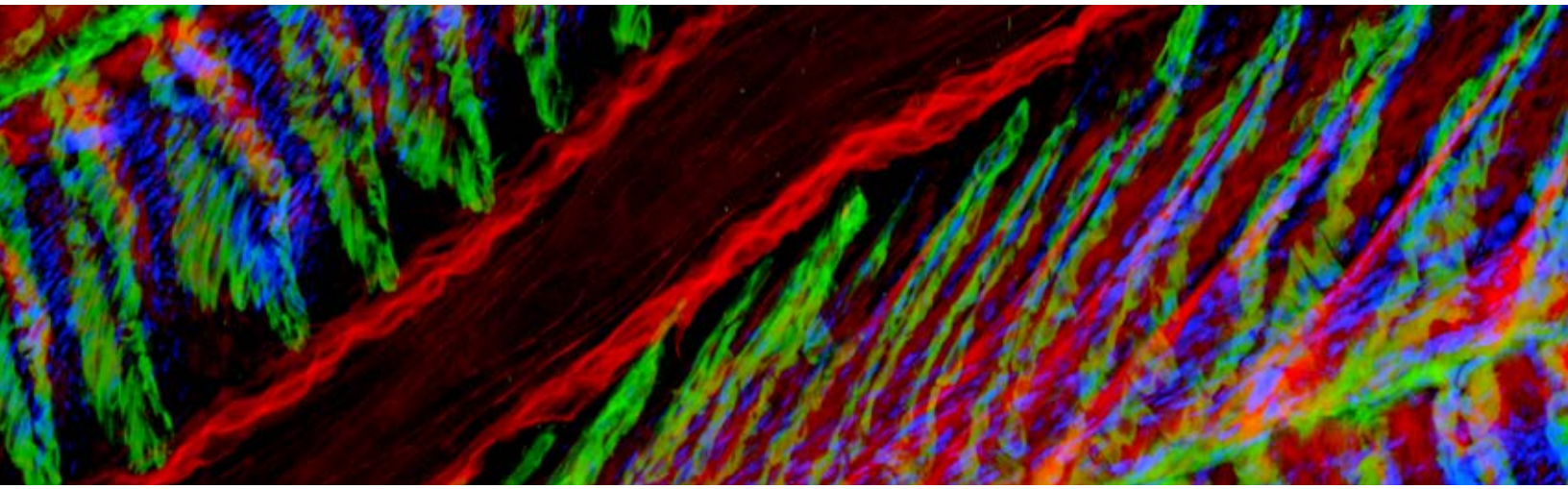

ANNUAL RESEARCH RETREAT

2025

SYNERGIES THAT ACCELERATE DISCOVERY

OCTOBER 17, 2025

The Inn at Swarthmore
Swarthmore, PA

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COVER PHOTO:

Equine lamellar tissue after tissue clearing and staining with anti-Keratin14, WGA (Wheat Germ Agglutinin), and Hoechst dye. Tissue and reagents for labeling provided by Hannah Galantino-Homer. Imaged by Gordon Ruthel on the Leica SP8-MP confocal/mutiphoton microscope in the Imaging Core.

PROGRAM

8:30 a.m.	**REGISTRATION & CONTINENTAL BREAKFAST**	
9:00 a.m.	**OPENING REMARKS**	Phillip Scott, PhD *Vice Dean for Research & Academic Resources*
9:20 a.m.	**SYNERGIES THAT ACCELERATE DISCOVERY IN LARGE ANIMAL VETERINARY MEDICINE** **Talk:** 12 min with 3 min Q & A	Introduction by Katrin Hinrichs, DVM, PhD, DACT *(5 min)*
9:25 a.m.	Cases, clients, and collaboration: the EDM story	Amy L. Johnson, DVM, DACVIM
9:40 a.m.	**THE INSTITUTE FOR INFECTIOUS & ZOONOTIC DISEASES: SUPPORTING BASIC AND CLINICAL INFECTIOUS DISEASE RESEARCH AND EDUCATION AT PENN VET** **Talks:** 12 min with 3 min Q & A	Introduction by Christopher A. Hunter, PhD *(5 min)*
9:45 a.m.	The ecology and spread of the North American H5N1 panzootic	Louise H. Moncla, PhD
10:00 a.m.	One Health investigations into transmission of carbapenemase-producing organisms	Stephen D. Cole, VMD, MS, DACVM
10:15 a.m.	**BREAK**	
10:30 a.m.	**ROBERT R. MARSHAK LECTURE** David F. Meaney, PhD Vice Provost for Research **Talk:** 40 min with 10 min Q & A	Introduction by Phillip Scott, PhD *(5 min)*
10:35 a.m.	Using extracellular vesicles as a window into brain recovery after concussion	David F. Meaney, PhD *Vice Provost for Research* *Solomon R. Pollack Professor of Bioengineering*
11:25 a.m.	**PENN VET CORES LIGHTNING SESSION** **Talks:** 3 min	Introduction by Phillip Scott, PhD *(5 min)*
11:30 a.m.	Imaging Core	Bruce D. Freedman, VMD, PhD
	Animal Model Core–New Bolton Center	Thomas Schaer, VMD, PhD
	Extracellular Vesicles Core Facility	Luca Musante, MS, PhD
	Center for Host-Microbial Interactions (Bioinformatics Support)	Lisa Mattei, PhD
	Transgenic Mouse Core	N. Adrian Leu
	Comparative Pathology Core	Arin Cox, DVM, DACVP
11:55 a.m.	**LUNCH & POSTER SESSION**	

PROGRAM CONT'D.

1:30 p.m.	**INVITED SPEAKER** Scott E. Hensley, PhD Professor of Microbiology **Talk:** 25 min with 5 min Q & A	Introduction by Louise H. Moncla, PhD *(5 min)*
1:35 p.m.	Development of avian influenza mRNA-LNP vaccines for humans and livestock	Scott E. Hensley, PhD *Professor of Microbiology* *Director, Penn Center of Excellence for Influenza Research and Response*
2:05 p.m.	**PENN VET CANCER CENTER: SYNERGY THROUGH CONVERGENCE** **Talks:** 12 min with 3 min Q & A	Introduction by Ellen Puré, PhD *(5 min)*
2:10 p.m.	Rewiring immunity with iNKT cells	Antonella Rotolo, MD, PhD
2:25 p.m.	APC: new insights into an old tumor suppressor	Christopher J. Lengner, PhD
2:40 p.m.	**BREAK**	
2:55 p.m.	**SYNERGIES IN SMALL ANIMAL MEDICINE** **Talks:** 12 min with 3 min Q & A	Introduction by Mark Oyama, DVM, MSCE, DACVIM *(5 min)*
3:00 p.m.	Accelerating translation of intraoperative near-infrared imaging	David Holt, BVSc
3:15 p.m.	A pilot, canine clinical trial using anti-inflammatory microcapsules following cranial cruciate ligament injury	Kimberly A. Agnello, DVM, DACVS, DACVSMR
3:30 p.m.	**SYNERGIES AT THE CENTER FOR STEWARDSHIP AGRICULTURE & FOOD SECURITY** **Talks:** 12 min with 3 min Q & A	Introduction by Thomas D. Parsons, VMD, PhD, DACAW *(5 min)*
3:35 p.m.	Agroforestry: realizing the potential of NBC as a living laboratory to study the interface of animal agriculture and the natural world	Thomas D. Parsons, VMD, PhD, DACAW
3:50 p.m.	Research storylines at the nutrition and metabolism lab	Eduardo Rico, PhD
4:05 p.m.	**ZOETIS PRIZE**	Awarded by Igor E. Brodsky, PhD
4:15 p.m.	**RECEPTION**	

ACKNOWLEDGMENTS

Organizing Committee

Phillip Scott, PhD
Katherine A. Kruger, MSW

THE UNIVERSITY OF PENNSYLVANIA SCHOOL OF VETERINARY MEDICINE IS GRATEFUL TO THE ORGANIZATIONS, SPONSORS, DONORS, AND FAMILIES WHO HAVE MADE OUR RESEARCH POSSIBLE.

Zoetis

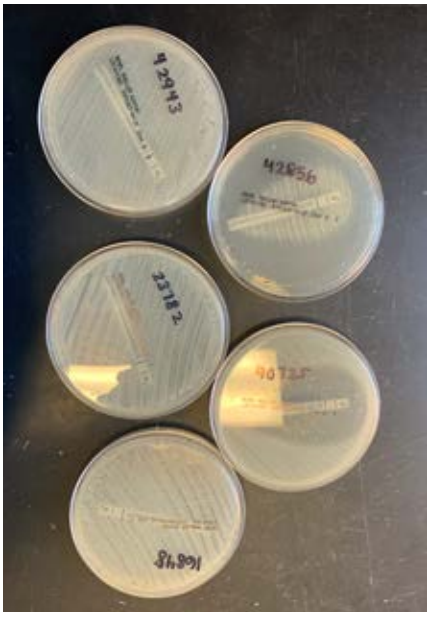
Our thanks to Zoetis for the 2025 Zoetis Award for Veterinary Research Excellence to be presented to a member of the Penn Vet faculty. The award aims to foster innovative research by recognizing outstanding research effort and productivity in the veterinary profession.

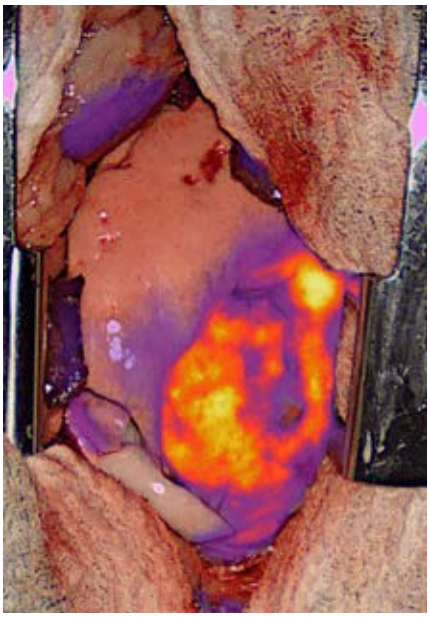
Robert R. Marshak Lectureship

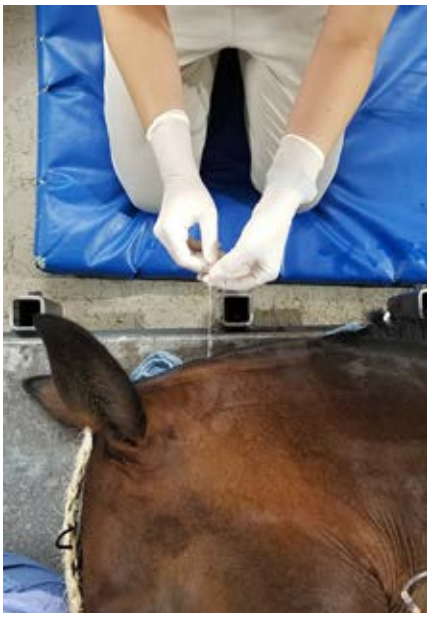
We are grateful to the memory of Dean Emeritus Robert R. Marshak, who was the dean of the School of Veterinary Medicine from 1973 to 1987. He was a visionary leader of the profession and a pioneer of bovine practice.

Thank You

We thank our generous and helpful friends and colleagues, including Sue Waddington-Pilder; Mary Berger; Laura H. Brown; John Donges; Rita Giordano; Marty Hackett; Ashley Hinton; Colin Redick; Stephen Hawkins; Gordon Ruthel; Melissa Sage, Inn at Swarthmore; and Anne Marie Kane, Imogen Design, LLC.







PHOTOS (FROM TOP TO BOTTOM):

1. High-level mupirocin resistance assay results for strains of *Staphylococcus haemolyticus* isolated from animals (Stephen Cole)
2. Near infrared imaging of a canine primary lung tumor using a choline kinase linked fluorophore (David Holt)
3. Preparing to collect samples of cerebrospinal fluid via atlanto-occipital approach from a horse with neurologic disease (Amy Johnson)

ROBERT R. MARSHAK LECTURE

THE ROBERT R. MARSHAK LECTURESHIP WAS ESTABLISHED IN 1993 IN HONOR OF DEAN EMERITUS ROBERT MARSHAK, THE NINTH DEAN OF THE SCHOOL OF VETERINARY MEDICINE.

David F. Meaney, PhD

DAVID F. MEANEY, PhD

Vice Provost for Research
Solomon R. Pollack Professor of Bioengineering
University of Pennsylvania

Using extracellular vesicles as a window into brain recovery after concussion

David F. Meaney, PhD, is the Solomon R. Pollack Professor of Bioengineering and Vice Provost for Research at the University of Pennsylvania, where he directs Penn's $1.4 billion research enterprise. A faculty member since 1993, he has held multiple leadership roles, including Senior Associate Dean of Penn Engineering and Chair of Bioengineering, where he oversaw major capital expansions, launched cross-disciplinary initiatives, and helped elevate the department to a top-five national ranking.

An internationally recognized expert on traumatic brain injury and neural mechanobiology, Prof. Meaney has published more than 150 papers with over 20,000 citations. His lab's work reshaped federal motor vehicle safety standards, saving thousands of lives each year, and led to new diagnostic and therapeutic technologies, including the founding of Axonova Medical. He is a fellow of AIMBE and BMES and the recipient of numerous honors, including the NSF CAREER Award and the Y.C. Fung Young Investigator Award.

INVITED SPEAKER

Scott E. Hensley, PhD

SCOTT E. HENSLEY, PhD

Professor, Department of Microbiology
Director, Penn Center of Excellence for Influenza Research and Response
University of Pennsylvania

Development of avian influenza mRNA-LNP vaccines for humans and livestock

Scott E. Hensley, PhD, is a Professor of Microbiology at the University of Pennsylvania and Director of the NIH-sponsored Penn Center of Excellence for Influenza Research and Response. He received his BA in biology from the University of Delaware in 2000 and his PhD in cell and molecular biology from the University of Pennsylvania in 2006. He completed a postdoctoral fellowship at the National Institutes of Health from 2007–2010, and was an Assistant Professor at the Wistar Institute from 2010–2016 and an Associate Professor at the University of Pennsylvania from 2016–2021. The Hensley laboratory studies mechanisms that promote antigenic drift of influenza viruses and factors that influence influenza vaccine responsiveness. During the COVID-19 pandemic, the laboratory launched several new serological assays to characterize immune responses elicited by SARS-CoV-2 vaccinations and infections. Finally, the laboratory has developed new mRNA-based vaccines to elicit broad immune responses against influenza viruses and SARS-CoV-2 variants.

PENN VET SPEAKERS

Kimberly A. Agnello, DVM, DACVS, DACVSMR

Dr. Agnello is a professor of surgery in the Department of Clinical Sciences and Advanced Medicine. Dr. Agnello earned her DVM degree from Cornell University and a MS degree from the University of New York at Buffalo, Roswell Park Cancer Institute. She completed her small animal surgery residency at the University of California, Davis and a postdoctoral research fellowship at the University of Georgia. She has dual board certification from the American College of Veterinary Surgeons and the American College of Veterinary Sports Medicine and Rehabilitation. She is a founding fellow in minimally invasive orthopedics through the American College of Veterinary Surgeons and is an AO North America faculty member. Her research involves using the dog as a translational model of naturally occurring osteoarthritis and serves as the clinical trials liaison at the Veterinary Clinical Investigations Center (VCIC) at the University of Pennsylvania.

Stephen D. Cole, VMD, MS, DACVM

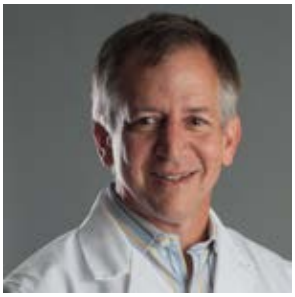
Dr. Cole is an assistant professor of microbiology and director of the Clinical Infectious Disease Laboratory at Penn Vet. He earned his Master of Science in Microbiology from the College of William & Mary in 2011 and his VMD from Penn Vet in 2015.

Dr. Cole is board-certified in bacteriology (2018), immunology (2018), and virology (2020) by the American College of Veterinary Microbiologists. His contributions to the field have been recognized with numerous honors, including the ASM Peggy Cotter Early Career Award, multiple teaching awards, and designation as a One Health Scholar by the AAVMC.

His research centers on understanding and mitigating the transmission of antibiotic-resistant bacteria between companion animals and humans, with a focus on advancing One Health approaches to infectious disease diagnosis and control.

Arin Cox, DVM, DACVP

Dr. Cox is a veterinary pathologist at the Comparative Pathology Core (CPC). He received his DVM from Mississippi State University and went on to pursue a postdoc at the University of Iowa, where he studied visceral leishmaniasis and tick-borne disease in hunting dogs. He completed his residency in veterinary anatomic pathology at the Ohio State University in 2024, along with his MSc studying genetic markers in thyroid cancer. After residency, he pursued additional training in comparative pathology as a fellow at the CPC, under the mentorship of Drs. Enrico Radaelli and Charles-Antoine Assenmacher. His research interests are broad and encompass cellular immunotherapies, infectious disease immunology, FLASH radiation, and more, and he has a special interest in collaborating with researchers to translate animal model studies to clinical trials.



Bruce D. Freedman, VMD, PhD

Dr. Freedman is an associate professor of pathobiology in the School of Veterinary Medicine. His research focuses on the mechanisms of signal transduction in immune cells, with particular emphasis on how intracellular calcium signals, triggered by antigen engagement, regulate lymphocyte fate and function. He maintains a long-standing collaboration with Dr. Michael May in the Department of Biomedical Sciences to investigate how calcium signals regulate the transcription factor NF-kB. More recently, he has partnered with Dr. Roderick O'Connor in the School of Medicine to explore strategies for enhancing calcium signaling and mitochondrial vitality to strengthen CAR T cell function in the hostile solid tumor microenvironment. For the past 15 years, Dr. Freedman has also directed the PennVet Imaging Core, a shared resource equipped with a broad range of state-of-the-art microscopes that are available to all faculty across the School of Veterinary Medicine and the wider university community.

Katrin Hinrichs, DVM, PhD, DACT

Dr. Hinrichs is the Harry Werner Endowed Professor of Equine Medicine and chair of the Department of Clinical Studies–New Bolton Center. She obtained her DVM from UC Davis and her PhD from the University of Pennsylvania, after completing a residency in large animal reproduction at New Bolton Center. She served on the faculty at Tufts University and Texas A&M University before returning to Penn in 2020. Her laboratory has pioneered research in equine assisted reproduction, including cloning, embryo biopsy and embryo vitrification, and developed methods for clinical application of ICSI that are now utilized worldwide. Most recently, her laboratory published the first efficient protocol for standard equine IVF.

David Holt, BVSc

Dr. Holt graduated with a Bachelor of Veterinary Science from the University of Sydney in 1983 and worked in private practice in Australia. He completed an internship and surgery residency at the University of Pennsylvania School of Veterinary Medicine in 1990. He is currently professor of surgery and a diplomate of the American College of Veterinary Surgeons. His research interests include imaging cancer during surgery.

PENN VET SPEAKERS

Christopher A. Hunter, PhD

Dr. Hunter is the director of the Institute for Infectious & Zoonotic Diseases (IIZD) and has been a member of the Penn Vet faculty for 30 years. His research centers on understanding how the immune system balances protective and pathological responses during infection.

Amy L. Johnson, DVM, DACVIM

Dr. Johnson began her time at Penn as an undergraduate biology major (C'99) but then headed north for the gorges of Ithaca, graduating from Cornell University College of Veterinary Medicine in 2003. She then completed an equine internship (B.W. Furlong and Associates, 2004), large animal internal medicine residency (Cornell, 2007), and neurology residency (Penn, 2011). In 2011, she became the first American board-certified large animal neurologist and joined Penn Vet's faculty, in which she is now a professor of large animal medicine and neurology (CE track) and the Marilyn M. Simpson Professor of Equine Medicine. Dr. Johnson's research focuses on improving antemortem diagnosis of neurological diseases in horses, with a current focus on neurodegenerative disease.

In her spare time she serves as chauffeur extraordinaire and field hockey coach for her three children and many others.

Christopher J. Lengner, PhD

Dr. Lengner is the Harriet Ellison Woodward Professor and chair of the Department of Biomedical Sciences, where his lab uses molecular genetic and genomic tools to understand the organization of adult stem cell compartments and their oncogenic transformation. The Lengner lab currently focuses on endodermal organs and disease states, including understanding the fundamental organization of the intestinal stem cell compartment and how its dysregulation initiates tumorigenesis, how telomere biology disorders impact stem cell function and crosstalk with the microenvironment, and how new genetic tools can be harnessed to understand lineage in tissue regeneration and cancer metastases.

Prior to assuming the role of department chair, Dr. Lengner acted as the co-director, along with Dr. Jeremy Wang, of Penn Vet's Center for Animal Transgenesis from 2014-2023. Dr. Lengner also served as the associate director of the Institute for Regenerative Medicine at the University of Pennsylvania from 2017-2023.

No Photo Available

N. Adrian Leu

Adrian Leu is the director of the Penn Vet Transgenic Facility and brings over 20 years of experience in generating transgenic mice. His expertise in microinjection techniques has enabled him to successfully clone mice using somatic cell nuclear transfer. In addition to producing numerous mice using the Intracytoplasmic Sperm Injection (ICSI) method, his passion for reproductive science has led him to successfully generate both a kitten and a horse foal using ICSI.

Lisa Mattei, PhD

Dr. Mattei is a senior research investigator in the Center for Host-Microbial Interactions (CHMI), part of the Institute for Infectious and Zoonotic Diseases (IIZD) at Penn Vet. She received her Bachelor of Arts from Bryn Mawr College, with a major in biology at Haverford College, and her PhD in 2012 from Yale University. During her doctoral training in the laboratory of Dr. Akiko Iwasaki, she studied innate immune responses to DNA viruses and the regulation of adaptive immunity through lymph node remodeling. Following her postdoctoral work in the Molecular Diagnostics Laboratory at Yale-New Haven Hospital, where she gained expertise in microbiome sequencing, she directed the Sequencing Core at the CHOP Microbiome Center from 2015–2021. Her current research at CHMI focuses on the use of microbiome and microbial sequencing approaches to investigate host–microbe interactions. Ongoing projects include studies of antimicrobial resistance in the Galápagos Islands, white-nose syndrome in Pennsylvania bats, and the upper airway microbiome in children with pneumonia. For the past year, she has also played a key role in the operations of IIZD.

Louise H. Moncla, PhD

Dr. Moncla's research focuses on using genomic approaches to understand RNA virus emergence, evolution, and transmission, with a particular focus on highly pathogenic avian influenza viruses. Her lab draws on approaches from virology, phylodynamics, and population genetics to study how emerging and re-emerging RNA viruses cross species barriers and evolve in different host populations. Ultimately, the goal of her work is to inform public health interventions to reduce the burden of emerging viruses on humans and animals.

PENN VET SPEAKERS

Luca Musante, MS, PhD

Dr. Musante has built a career at the intersection of protein biochemistry, kidney disease, and extracellular vesicle (EV) biology, establishing himself as a leading innovator in the field. His early work dissected the biochemical mechanisms of glomerular permeability and proteinuria, providing insights into the molecular imbalances that drive nephrotic syndrome. This foundation in protein pathophysiology set the stage for his long-standing focus on extracellular vesicles as powerful biomarkers and mediators of disease.

As the director of the Extracellular Vesicles Core Facility at the University of Pennsylvania, Dr. Musante leads a dynamic resource dedicated to empowering researchers across disciplines to harness EVs in their work. He has introduced state-of-the-art instrumentation such as nano-flow cytometry and established workflows for high-quality EV isolation, characterization, and functional studies. Under his leadership, the Core not only provides technical expertise but also fosters collaboration, mentorship, and methodological rigor, ensuring that investigators can confidently integrate EVs into their experimental designs.

Mark Oyama, DVM, MSCE, DACVIM

Dr. Oyama is chair of the Department of Clinical Sciences and Advanced Medicine and a board certified veterinary cardiologist. Dr. Oyama received his DVM degree from the University of Illinois in 1994, performed an internship at The Animal Medical Center in NYC, and a cardiology residency at the University of California at Davis. Dr. Oyama holds a master's degree in clinical epidemiology from the Center for Clinical Epidemiology and Biostatistics at PSOM. He has published over 120 peer reviewed research papers and 90 scientific abstracts. He has obtained over 80 grants, contracts, and sponsored research funds from a variety of sources, including industry, foundation, state and federal. He has been fortunate to deliver over 100 lectures at various professional meetings all over the world. Dr. Oyama is particularly interested in pathophysiology of mitral valve degeneration and performing clinical trials of new pharmaceuticals for heart failure in the dog and cat.

Thomas D. Parsons, VMD, PhD, DACAW

Dr. Parsons is the Marie A. Moore Endowed Chair in Animal Welfare and Ethics at the University of Pennsylvania School of Veterinary Medicine. He is also the director of Penn Vet's Swine Teaching and Research Center and is heading the development of a new Center for Stewardship Agriculture and Food Security. His work focuses on advancing sustainable models of agriculture through the study of animal behavior, health, welfare, and applications of technology. Dr. Parsons' interest in agriculture is longstanding, as he was raised on a family farm in western Massachusetts, where his nephew, Christopher, is the 10th generation of Parsons to work land deeded from King George of England. As a faculty member at Penn Vet, Dr. Parsons has built one of the largest research groups working on farm animal welfare in North America.

Ellen Puré, PhD

Dr. Puré is the founding director of the Penn Vet Cancer Center, is the Grace Lansing Lambert Professor and former chair of the Department of Biomedical Sciences at the School of Veterinary Medicine, and professor of systems pharmacology and translational therapeutics at the Perelman School of Medicine at the University of Pennsylvania. Dr. Puré received her baccalaureate degree from Washington University in St. Louis, and her doctorate from the University of Texas-Southwestern Medical School. She trained as a Damon Runyon-Walter Winchell Postdoctoral Fellow and Leukemia Society Special Fellow and then joined the faculty at the Rockefeller University. In 1992, Dr. Puré moved to Philadelphia where she was on the faculty of the Wistar Institute until moving to the University of Pennsylvania in 2013. Dr. Puré is an associate director of the Cancer Research Institute and currently serves on the editorial boards of the *Journal of Clinical Investigation* and is a founding senior editor of *Cancer Immunology Research*.

Dr. Puré's research focuses on the cellular and molecular basis of inflammation and fibrosis. She studies basic mechanisms involved in these processes and the contribution of these processes to fibrotic diseases and cancer. Her laboratory has made seminal contributions to our understanding of the roles of stromal cells and extracellular matrix remodeling in tissue fibrosis and in cancer risk, initiation, progression, and metastasis. Her lab is developing novel therapeutic approaches to target stroma to treat fibrosis and cancer. In 2019, Dr. Puré was named a Fellow in the American Association for the Advancement of Science (AAAS). Dr. Puré co-founded Capstan Therapeutics in 2021.

Eduardo Rico, PhD

Dr. Rico is an assistant professor of population medicine, sustainable agriculture, and food security, in the Department of Clinical Studies–New Bolton Center at Penn Vet. Following his work as an applied nutritionist in his home country of Colombia, Dr. Rico completed master's and doctoral studies in the United States. After completing postdoctoral training at Cornell University, Dr. Rico held a three-year appointment as an assistant professor at the University of Maryland before joining the faculty at the University of Pennsylvania in 2024.

Currently, his research centers on studying the impacts of nutrition on nutrient metabolism and health of animals, with a particular focus on the dairy cow. Areas of current interest include investigation of the primary causes of metabolic dysfunction at the onset of lactation and during obesity, the use of nutritional approaches for the control of inflammation, and the evaluation of novel feed ingredients for sustainable animal food production systems.

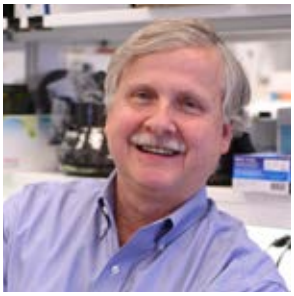
PENN VET SPEAKERS

Antonella Rotolo, MD, PhD

Dr. Rotolo is a research assistant professor of immunobiology at the University of Pennsylvania School of Veterinary Medicine. Her research focuses on developing off-the-shelf iNKT cell-based therapies for cancer and immune-mediated diseases. She earned her MD from the University of Turin in Italy, a PhD in immunology from Imperial College London in the UK, and completed her postdoctoral training in cellular therapy and comparative immunology at the University of Pennsylvania. Her work led to the development of a dual-specific CAR-iNKT cell platform for the treatment of refractory B-cell lymphomas, including those resistant to conventional CAR T-cell therapies. Now in clinical development, this platform is also being explored for applications in solid tumors. At Penn Vet, Antonella established the first canine iNKT model to bridge the gap between mouse preclinical studies and human clinical trials. She is currently investigating the safety and efficacy of off-the-shelf, unedited CAR-iNKT cells from healthy dogs in MHC-unmatched canine patients with refractory, metastatic osteosarcoma. Committed to advancing iNKT cell therapies globally, Antonella founded and chairs the Consortium for iNKT Research and Therapy. Her goal is to promote iNKT discoveries and ultimately harness their effector, immunomodulatory, and off-the-shelf potential to develop more effective, universal cellular therapies for patients with as-yet incurable cancers and immune-mediated diseases worldwide.

Thomas Schaer, VMD, PhD

Dr. Schaer is a large animal surgeon at the University of Pennsylvania School of Veterinary Medicine's New Bolton Center, with over 15 years of experience taking products from concept to commercialization. In 2005, he launched a product development platform focused on preclinical and regulatory sciences, bringing together multidisciplinary teams from academia and industry. To date, this ecosystem has served as a sandbox for over 120 Pre-Vet students, more than 40 surgery fellows, numerous graduate students, and many visiting researchers. His lab's fingerprints are on over 16 therapies and devices that have gone on to successful clinical launches. His greatest passion is training the next generation of clinician scientists in musculoskeletal research and surgical innovation. He is passionate about biofilm infections and currently enjoys introducing new techniques and concepts developed for human patients in spine care and joint reconstruction to veterinary patients.



Phillip Scott, PhD

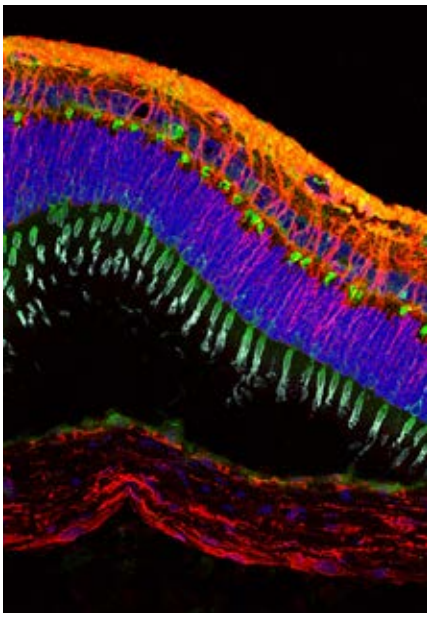
Dr. Scott is a professor of microbiology and immunology in the Department of Pathobiology and serves as the vice dean for research and academic resources at Penn Vet. His research focuses on understanding the development, regulation, and maintenance of protective and pathologic CD4+ and CD8+ T cells in order to design new vaccines and immunotherapies for infectious diseases, with a primary emphasis on cutaneous leishmaniasis. The Scott laboratory currently focuses on three main areas: 1.) Defining the role of CD8+ T cells in mediating increased pathology and using that information to develop immunotherapies to accelerate healing in cutaneous leishmaniasis patients; 2.) Defining how dermal CD4+ T resident memory cells develop and are maintained, with the goal of targeting them in vaccine strategies; 3.) Understanding how the skin microbiome influences immune responses to leishmaniasis. Dr. Scott earned his PhD in parasitology from the University of Pennsylvania (1980).

PENN VET CORES

PENN VET'S RESEARCH FACILITIES INCLUDE STATE-OF-THE-ART CORE LABORATORIES ON BOTH THE PHILADELPHIA AND NEW BOLTON CENTER CAMPUSES, AND OFFER RESEARCHERS THROUGHOUT THE UNIVERSITY OF PENNSYLVANIA THE OPPORTUNITY TO USE HIGHLY SPECIALIZED TECHNOLOGY AND BENEFIT FROM THE EXPERTISE OF WORLD-CLASS PATHOLOGISTS.

In the following pages, you can learn about the services and synergies available through Penn Vet's core laboratories.

- Animal Model Core–New Bolton Center
- Center for Host-Microbial Interactions (CHMI)(Bioinformatics Support)
- Comparative Pathology Core
- Extracellular Vesicles Core Facility (EVs Core)
- PennVet Imaging Core (PVIC)
- Transgenic Mouse Core



PHOTOS (FROM TOP TO BOTTOM):

1. *Leishmania* imaged from the work of Fernanda Novais in the laboratory of Phillip Scott. Imaged by Gordon Ruthel using a widefield epifluorescence microscope in the Imaging Core.
2. Hookworms from the work of Annabel Ferguson in the laboratory of De'Broski Herbert. These hookworms were imaged with extended depth of focus brightfield microscopy by Gordon Ruthel on the Leica DM6000 microscope in the Imaging Core.
3. Canine retina from the work of Karina Guziewicz in the laboratories of Gus Aguirre and William Beltran, imaged by Gordon Ruthel on the Leica SP5 confocal microscope in the Imaging Core.

PENN VET CORES

ANIMAL MODEL CORE–NEW BOLTON CENTER

CORE LEADERSHIP & MANAGEMENT

Thomas P. Schaer, VMD, Associate Professor of Comparative Orthopaedic Surgery, Clinical Studies–NBC
Luis Ramon, DVM, GLP Study Director, Clinical Studies–NBC
Shamim Naghdi, PhD, GLP Quality Assurance & Molecular Techniques, Clinical Studies–NBC
Veridiana Nadruz, DVM, Internal Medicine & *in vivo* Gait Analyses

LOCATION & CONTACT INFORMATION

Location: New Bolton Center Campus CMK
Email: corl@vet.upenn.edu • **Phone:** 610 925 6237 • **Cell:** 484 620 9132
Website: https://www.vet.upenn.edu/research/research-laboratories/amc-corl/

CORE OVERVIEW

The Animal Model Core at Penn Vet New Bolton Center is an ecosystem for medical translation and multidisciplinary collaboration. It leads and supports discovery, invention, and innovation in medical product development across a broad range of disciplines. The AMC-CORL group leads, supports, and collaborates on many federal and industry-funded projects at the intersection of science and the rapid advancements in healthcare technology. This multidisciplinary collaboration provides an immersive experience for mentoring of graduate and undergraduate students in the translational and regulatory sciences through our unique training opportunities. The core is staffed by four to five veterinarians with surgical experience, a Study Director (GLP), a Quality Assurance and Quality Control Officer (GLP), two to three research technicians, and five to ten research assistants. Our staff are responsible for day-to-day operations (24/7 365 days a year), project design and management, animal care, data collection, and evaluation of *in vivo* and *ex vivo* components of a given study.

Our **SERVICE CORE** designs and executes studies from proof of concept to pivotal IND/IDE-enabling trials (GLP/VICH-9) in support of raising R&D capital and regulatory submissions, and offers a wide variety of animal models.

Our **RESEARCH CORE** initiates and collaborates with academia on hypothesis-driven research using animal models in support of investigations in regenerative medicine, tissue engineering, orthopedic trauma, spinal deformities, microbial-host interactions, wound healing, and biofilm infections.

SERVICES & CAPABILITIES

- Project Planning / Grant Development (SBIR, DOD, NIH, NSF)
- Over 60 approved programmatic IACUC Protocols
- Test Article Prototyping & Testing (GLP/ISO10993)
- Model Development & Refinement
- Feasibility, Pilot & Pivotal Studies (GLP/21CFRpart58)
- Planning & Execution of IND/IDE Enabling-Studies
- Acute & Chronic Studies
- Animal Models with Comorbidities, Biofilm & Total Joint Replacement, Periprosthetic Joint Infections (knee, hip & spine)
- Histology Services

ACCESS INFORMATION

Who Can Access:
We collaborate with internal and external labs, start-ups, and established biotech firms.

How to Get Started:
Contact: corl@vet.upenn.edu, tpschaer@vet.upenn.edu, lramon@vet.upenn.edu

Training & Support:
We host PIs, trainees, learners at any level, and sponsors during clinical procedures to support and enrich their experience in a cross-functional team setting. One of the foundational tenets of our lab is to foster the growth of the next generation of scientists and researchers. Through our programs, we support undergraduate and post-doctoral students in their professional and intellectual development, providing mentorship and hands-on opportunities in the field of translational research.

PRICING & FUNDING

Fee Structure:
Not subsidized. Fee structure at cost plus applicable F&A per https://researchservices.upenn.edu/resources/penn-data-for-proposals/ for Federal- and Industry-funded projects.

RECENT HIGHLIGHTS OR IMPACT

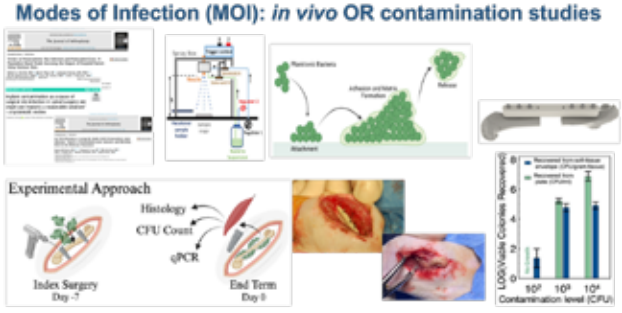
Notable Projects or Discoveries:
Our work has resulted in six published patents and the global clinical launch of over 16 new technologies, most recently for spinal muscular atrophy in children (PIERRE Trial, NCT06555419), intervertebral disc augmentation (HYDRAFIL-D Trial, NCT06011551), and smart devices in spinal pedicle instruments (https://waypointorthopedics.com/).

Publications or Awards:

Publications: https://www.ncbi.nlm.nih.gov/myncbi/thomas.schaer.2/bibliography/public/

2023 American Society of Mechanical Engineers Edward Grood Interdisciplinary Team Science Medal in Bioengineering

FUTURE DIRECTIONS OR UPGRADES



The microbial colonization of tissue-contacting biomedical devices begins with the microbial adherence to the device surface. One potential contamination source is the surgical operating room, where viable bacteria in the OR atmosphere can settle onto a device surface during surgery. Enhanced infection-control practices have reduced sedimentation rates to approximately 10^3-10^4 CFU/m^2/h; however, a strong clinical consensus remains that OR contamination is associated with device infections. To simulate OR contamination, we have been developing **an aerosolizing system capable of spraying small amounts of bacteria onto surfaces**. This system utilizes brief bursts of pressurized gas to aerosolize liquids—typically buffer solutions containing a known bacterial concentration—with volumes ranging from approximately 10 to 200 μL. These bursts can contaminate implant surfaces with bacterial densities on the order of 10^2 CFU/cm^2. Moving towards *in vivo* assessment, preliminary experiments indicate that unmodified Ti surfaces contaminated using the spray system can reproducibly provoke infection in a rat femur model at concentrations ranging from 10^2-10^6cfu.

PENN VET CORES

CENTER FOR HOST-MICROBIAL INTERACTIONS (BIOINFORMATICS SUPPORT)

CORE LEADERSHIP & MANAGEMENT

Director: Dan Beiting, PhD, Associate Professor of Pathobiology
Manager: Dan Cutillo
Staff Bioinformaticians: Rui Xiao, PhD and Andrew Hart, PhD
Staff Scientist: Lisa Mattei, PhD

LOCATION & CONTACT INFORMATION

Location: Hill Pavilion, Room 331
Contacts: Dan Beiting (beiting@vet.upenn.edu) & Dan Cutillo (dcutillo@vet.upenn.edu)
Websites: Find us on the Penn Vet Cores page (Research > Core Labs > CHMI) or at hostmicrobe.org

CORE OVERVIEW

Purpose and Mission:

The Center for Host-Microbial Interactions (CHMI), based at the Institute for Infectious and Zoonotic Diseases at Penn Vet, is a shared resource for high-throughput sequencing and data analysis. Our research focuses on the role of the microbial world in shaping the health of humans, animals, and the environment. We collaborate closely with researchers, veterinarians, and clinicians across Penn and beyond to provide expert training and technical support for the production and interpretation of complex genomic data.

Key Research Areas Supported:

- **Transcriptomics and Gene Expression:** Bulk and single-cell RNA sequencing for profiling expression dynamics across development, disease, and experimental conditions.
- **Metagenomics and Metatranscriptomics:** High-throughput sequencing of microbial communities to study diversity, function, and host-microbe interactions.
- **Pathogen Genomics and Infectious Diseases:** Genomic sequencing for pathogen identification, antimicrobial resistance, outbreak tracking, and host-pathogen interactions.

SERVICES & CAPABILITIES

Primary Services Offered:

- ***Free*** consultations and study design
- Bulk RNA-seq of tissues, cultures, or sorted cells
- 10x single-cell RNA-seq, CITE-seq, Multiome, Flex, and more!
- Untargeted 'shotgun' metagenomics for microbiome profiling or pathogen discovery
- Custom protocols (DNA & RNA, short- & long-read)
- Bioinformatics support:
  - Bulk, single-cell, & spatial RNA-seq
  - Shotgun metagenomics & metatranscriptomics
  - Genome assembly & annotation
  - 3D protein structures with AlphaFold3
  - Custom analysis

Specialized Equipment or Platforms:

NextSeq 2000, MinION,10X Chromium X and iX, Zephyr Automated Liquid Handler, TapeStation, QIAcube, Qubit, LUNA-FL Automated Cell Counter

Technical Expertise Available:

- **Andrew Hart:** immunology, single-cell and spatial RNAseq data analysis
- **Rui Xiao:** parasite genomics, computer programming, long-read analysis
- **Lisa Mattei:** microbiome study design and sequencing, long-read sequencing

ACCESS INFORMATION

Who Can Access:

We collaborate with researchers at Penn, Wistar, and CHOP, as well as with external academic institutions and industry partners.

How to Get Started:

Request a consultation with Dan Beiting and a quote from Dan Cutillo.

Training & Support:

CHMI offers full training and support for researchers who wish to carry out their own library preparation and sequencing.

PRICING & FUNDING

Fee Structure:

- **Tier 1 - $ -** customers do all the work; CHMI provides reagents and equipment.
- **Tier 2 - $$ -** customers do most of the work; CHMI provides reagents, equipment, and guidance.
- **Tier 3 - $$$ -** CHMI does all the work and provides all reagents, equipment, and labor.

PENN VET CORES

COMPARATIVE PATHOLOGY CORE

CORE LEADERSHIP & MANAGEMENT

Faculty Directors: Enrico Radaelli/Charley Assenmacher
Technical Director: Esha Banerjee
Department: Pathobiology

LOCATION & CONTACT INFORMATION

Location: Rosenthal building, Room 426 (CPC Lab); Ryan Hospital building, Room 4001 (Histology Lab)
Email: comppathologycore@vet.upenn.edu
Website: https://www.vet.upenn.edu/research/core-labs/comparative-pathology-core/

CORE OVERVIEW

Purpose and Mission:

The main goal of the CPC is to provide expert pathological characterization of experimental animal models for investigators performing *in vivo* studies as part of their basic and translational research endeavors. To accomplish its mission, the CPC offers the expertise of board-certified veterinary pathologists and access to a state-of-the-art pathology laboratory. Bridging the divide between natural and experimental diseases, the CPC investigates the disease processes of domestic and experimental animals and their translational value for specific human and companion animal conditions.

Key Research Areas Supported:

- Phenotyping of genetically engineered mice
- Toxicity/safety assessment and efficacy studies for cellular immunotherapies, gene therapies, etc.
- Clinical trials for companion animals from the MJ Ryan Veterinary Hospital

SERVICES & CAPABILITIES

Primary Services Offered:

- **Histology Service:** state-of-the-art pathology laboratory with processing, sectioning and staining of formal fixed, paraffin embedded, and frozen tissues.
- **Slide Evaluation Service:** pathological evaluation performed by Board-certified veterinary pathologists.
- **Complete Pathological Assessment:** autopsy with evaluation of all organs.
- **Molecular Staining Service:** chromogenic immunohistochemistry, immunofluorescence and ISH on FFPE or frozen sections; novel antibody/probe work-up.
- **Digital Pathology Service:** brightfield and IF scanning and digital image analysis of whole slides.
- **Pathology Consultations:** consultations for pathological endpoints or project planning.

Specialized Equipment or Platforms:

In addition to the fully equipped histology lab, the CPC has 2 automated **Leica BOND RXm** staining platforms and a **Leica Versa 200** slide scanner.

Technical Expertise Available:

The CPC technicians and pathologists are available for technical questions regarding tissue processing and staining, as well as for pathological interpretation of research samples.

ACCESS INFORMATION

Who Can Access:

Any investigator from Penn (Penn Vet, PSOM, etc.), CHOP, Wistar, or other academic institutions, as well as local and distant biotechs are welcome to use the CPC's services.

How to Get Started:

All information to create an account is available on the CPC website (see QR code below). For any additional information, investigators can email the CPC email address (comppathologycore@vet.upenn.edu).

PRICING & FUNDING

Fee Structure:

- A detailed overview of all fees is available on the CPC website.
- Penn/CHOP investigators receive discounted fees thanks to partial support from PSOM (ACC).

RECENT HIGHLIGHTS OR IMPACT

Notable Projects or Discoveries:

The CPC has worked in collaboration with numerous labs at Penn and CHOP to study the efficacy and toxicity of various cellular immunotherapies[1, 4], as well as gene therapy products[3, 5] and other basic research projects[6]. The CPC also helped clinician-scientists within Penn Vet to generate relevant data for their research in companion animals[2].

Publications or Awards:

1. Amit U, et al. Proton radiation boosts the efficacy of mesothelin-targeting chimeric antigen receptor T cell therapy in pancreatic cancer. *Proc Natl Acad Sci U S A.* 2024 Jul 30;121(31):e2403002121.
2. Bardales KL, et al. Intertumoral heterogeneity of the immune microenvironment in high grade canine mast cell tumors. *Vet Oncol.* 2025;2(1):7.
3. Castruccio Castracani, et al. An erythroid-specific lentiviral vector improves anemia and iron metabolism in a new model of XLSA. *Blood.* 2025 Jan 2;145(1):98-113.
4. Giudice AM, et al. D3-GPC2-directed CAR T cells are safe and efficacious in preclinical models of neuroblastoma and small cell lung cancer. *CCR.* In press.
5. Pyne NK, et al. Age-sensitive response of systemic AAV-mediated gene therapy in a newly characterized feline model of mucolipidosis II. *Mol Ther.* 2025 Aug 6;33(8):3808-3821.
6. Stewart DC, et al. Prognostic and therapeutic implications of tumor-restrictive type III collagen in the breast cancer microenvironment. *NPJ Breast Cancer.* 2024 Oct 2;10(1):86.

FUTURE DIRECTIONS OR UPGRADES

- Integration of Artificial Intelligence software in the Digital Pathology Service (HALO)
- Streamlined generation of TMAs
- Collaboration in the Spatial omics pipeline

Penn Vet | Comparative Pathology Core

PENN VET CORES

EXTRACELLULAR VESICLES CORE FACILITY

CORE LEADERSHIP & MANAGEMENT

Dean Andrew Hoffman, DVM, DVSc, DACVIM and **Dr. Luca Musante, MS, PhD**
Department: Dean's Office

LOCATION & CONTACT INFORMATION

Location: Rosenthal Building, Room 204/205
Email: musante@upenn.edu • **Phone:** 215-573-8215
Website: https://www.vet.upenn.edu/research/core-labs/extracellular-vesicle-core/

CORE OVERVIEW

The EV Core Facility provides researchers with reliable services for isolating, quantifying, and characterizing extracellular vesicles (EVs) and related nanoparticles. Our goal is to support high-quality, reproducible research by offering expertise in EVs, liposomes, lipid nanoparticles (LNPs), and viral particles such as lentivirus.

Core Services and Techniques:

- Isolation of EVs from biofluids, conditioned media, and connective tissue
- Quantification and size distribution analysis of EVs and related nanoparticles
- Phenotyping and marker quantification via nano-flow cytometry
- Molecular characterization of EV markers using electrophoresis and western blotting

Research Applications Enabled:

- Biomarker discovery and validation for diagnostics and prognostics
- Development and optimization of therapeutic nanoparticles (e.g., liposomes, LNPs, viral vectors)
- Mechanistic studies of cell-to-cell communication and signaling pathways
- Disease model investigations, including cancer, neurodegenerative disorders, and inflammation

SERVICES & CAPABILITIES

Extracellular Vesicle Isolation:

- Differential centrifugation and density gradient ultracentrifugation
- Size exclusion chromatography

Particle Quantification and Sizing:

- Microfluidic resistive pulse sensing (MRPS) with the nCS1 (Spectradyne)
- Nanoparticle tracking analysis (NTA) with the ZetaView (ParticleMetrix)

Single-Particle Characterization:

- Interferometric reflectance imaging sensing with ExoView Chip Array (Unchained Labs)
- Nano flow cytometry using nanoFCM (NanoFCM) or CytoFLEX nano (Beckman Coulter)

Scientific Support:

- Expert consultation on experimental design, workflows, and data interpretation

SPECIALIZED EQUIPMENT OR PLATFORMS:

Ultracentrifugation Systems:

- Optima L-90K ultracentrifuge with 45Ti, SW41, and SW55 rotors
- Optima TLX-120K benchtop ultracentrifuge with TLA 100.2 rotor

Particle Analysis and Characterization:

- nCS1 Microfluidic Resistive Pulse Sensing (Spectradyne)
- ZetaView PMX200 Nanoparticle Tracking Analysis (ParticleMetrix)
- ExoView Chip Array (Unchained Labs)
- NanoFCM flow cytometer (NanoFCM)
- CytoFLEX nano flow cytometer (Beckman Coulter)

Fractionation Platform:

- Automated size exclusion chromatography with fraction collector (Izon)

TECHNICAL EXPERTISE AVAILABLE:

Training:

- Hands-on instruction in EV isolation, quantification, and characterization methods
- Guidance on proper instrument operation and data acquisition
- Best practices for sample preparation and quality control

Technical Support:

- Direct assistance with experiments and workflows
- Troubleshooting of protocols, instrumentation, and data analysis
- Ongoing access to the EV Core Director for expert advice

Consultation:

- Study design and experimental planning tailored to research goals
- Optimization of protocols and selection of appropriate methodologies
- Interpretation of results to support robust and reproducible outcomes.

ACCESS INFORMATION

Who Can Access:
The EV Core Facility is open to academic and non-academic users, both internal and external. Depending on their needs, researchers may utilize the Core as a shared resource or request full-service support.

Contact the EV Core Director (Luca Musante) via email to arrange a consultation (remote or in-person) to discuss project needs, sample requirements, and service options.

First-time users will be required to complete training on any instrument they wish to operate. Comprehensive training and ongoing support are provided to ensure proper use of equipment and reliable data generation.

PRICING & FUNDING

User Type	Rate	Notes
Academic (internal & external)	Standard per-service fee	Rates vary depending on whether the Core is used as a shared resource or full-service support
Non-academic/Industry	Higher per-service fee	Rates also vary for resource vs. full service; contact the Core Director for a quote

RECENT HIGHLIGHTS OR IMPACT

Notable Projects or Discoveries:
Supported studies investigating EV-mediated delivery of therapeutic mRNA to the retina, advancing non-viral gene therapy approaches. Enabled mechanistic studies of neuronal stress and compensatory secretory pathways through precise EV isolation and characterization.

Publications or Awards:

1. Appelbaum et al., *Drug Delivery,* 2025 – Acknowledges EV Core assistance with ZetaView NTA measurements.
2. Chintapula et al., *Lab on a Chip,* 2025 – Credits EV Core support for nano flow cytometry analyses.
3. Baniel et al., *Cell,* 2025 – Recognizes technical support and consultation from the EV Core.
4. Palumbos et al., *PNAS,* 2025 – Thanks EV Core for extracellular vesicle isolation and analysis.

FUTURE DIRECTIONS OR UPGRADES

The EV Core Facility is actively exploring emerging technologies and commercial kits to make EV isolation and analysis faster, more precise, and more reproducible. Planned initiatives include high-throughput single-vesicle analysis platforms and enhanced isolation kits, with integrated workflows that leverage other Penn Core Facilities for specialized “omics” analyses and advanced sample preparation. These upgrades are expected to be available within the next 12–18 months.

PennVet IMAGING CORE

CORE LEADERSHIP & MANAGEMENT

Director: Bruce Freedman, VMD, PhD
Manager: Gordon Ruthel, PhD

LOCATION & CONTACT INFORMATION

Location: Hill Pavilion, Room 380
Email: goruthel@vet.upenn.edu • **Phone:** 215-746-0471
Website: https://www.vet.upenn.edu/research/core-labs/imaging-core/

CORE OVERVIEW

The PennVet Imaging Core (PVIC) was established in 2008 to meet the expanding microscopic imaging needs of faculty, postdocs, students, and research staff in the Penn Veterinary School, Penn Medical School, CHOP, WISTAR and surrounding communities. During the ensuing 15 years, with support from the Department of Pathobiology, laboratories in the SVM, the Dean's office of the SVM, the University of Pennsylvania Provost's office, and NIH, the PVIC has invested nearly 4 million dollars in cutting-edge microscope-based imaging technologies. The PVIC has a full time PhD-level expert to help users with all aspects of training and instrument use.

Key Research Areas Supported:

The PVIC has broad capability and provides full support for virtually any type of microscope-based imaging modality. Over the years, we have helped researchers in a wide range of efforts that include multiphoton, confocal, and widefield fluorescence imaging of live brain, lung, tumors, connective tissue, skin, gut, retina, and lymph nodes. We have helped with real time imaging of apoptosis and tumor cell killing, lymphocyte migration, the 2-D and 3-D structure of virtually every organ, real-time dynamics of protein-protein interactions, and dynamic measurements of virus budding from cells, to name a few. Finally, we have the capability to preform high content imaging (multi-well) to compare a range of experimental conditions (such as drug dose) on cell function and biology.

Our Expertise Includes but Is Not Limited To:

- Widefield/Brightfield imaging of live and fixed cells and tissues
- Widefield fluorescence imaging of live and fixed cells and tissue
- Confocal imaging (enhanced resolution up to ~125nM spatial resolution) of live and fixed tissues
- TIRF imaging of live and fixed tissues (principally used to look at membrane localization of molecules)

- Multiphoton/Intravital imaging of live and fixed tissues including brain, lymph nodes, lung, skin, etc.
- Super-resolution imaging of live and fixed tissues and cells (~25-50nM spatial resolution)
- Fluorescence lifetime imaging to assess protein-protein interactions
- Lifetime imaging in conjunction with spectral imaging to perform multiplex analysis (10 or more proteins or fluorescent molecules concurrently)
- Free support in designing experiments to be performed in the core. Free training and assistance with microscope operation and analysis.

SERVICES & CAPABILITIES

Microscopes and Imaging Methods Available Include:

- Leica SP8-MP confocal/multiphoton microscope: 2-photon, intravital, SHG (second harmonic generation) microscopy
- Leica Stellaris FALCON confocal/FLIM: Fluorescence Lifetime, FLIM-FRET, multiplex labeling and beginning in lat October of 2025, super-resolution microscopy
- Leica DM6000B widefield microscope: fluorescent or histological/chromogenic stains, image tiling
- Yokogawa spinning disk confocal: rapid live cell imaging
- GE DeltaVision OMX SI: structured illumination super-resolution, TIRF, deconvolution microscopy
- Molecular Devices ImageXpress Micro-4: High Content Imaging and Analysis

Image analysis software available on workstation computers includes Imaris, MetaMorph, Volocity, Huygens deconvolution, and off-line modules for Leica LASX with 3D capability.

ACCESS INFORMATION

Who Can Access:

The instruments and resources at the PennVet Imaging Core are available for the use of researchers across the University, the Philadelphia area, and beyond.

How to Get Started:

Penn researchers please register for the PennVet Imaging Core within CAMS: https://www.med.upenn.edu/apps/cams/access/spender_account_cores/new and contact the core manager (goruthel@vet.upenn.edu) for training on core instruments.

Training & Support:

Instrument-specific training is required prior to independent use of a core microscope. **Training and assistance are provided at no additional cost (other than microscope time).**

PRICING & FUNDING

Use of microscopes is charged at an hourly rate with no additional charge for training or assistance:

SP8-MP: $50/hour, **Stellaris:** $50/hour, **DM6000B:** $10/hour, **Spinning Disk Confocal:** $25 ($15 off-peak)/hour, **OMX:** $30 ($15 off-peak)/hour, **ImageXpress:** $25 ($15 off-peak)/hour, **STED (super-resolution):** TBD

FUTURE DIRECTIONS OR UPGRADES

tau-STED super-resolution capability will be implemented on the Leica Stellaris FALCON system in October. This allows real time visualization of tissue and cells with resolution of nearly 10 times greater than standard confocal microscopy.

PENN VET CORES

TRANSGENIC MOUSE CORE

CORE LEADERSHIP & MANAGEMENT

The Transgenic Mouse Core is part of the **Department of Biomedical Sciences.** It is operated by **Adrian Leu,** and **Stephanie Sterling.**

LOCATION & CONTACT INFORMATION

Location: Lab 195E, Old Vet Building
Email: nleu@upenn.edu • **Phone:** 215-573-2302
Website: https://www.vet.upenn.edu/research/core-labs/transgenic-mouse-core/

CORE OVERVIEW

Purpose and Mission:

Our mission is to support research at Penn and beyond by designing and generating novel transgenic mouse models. We also offer services for re-derivation of mouse strains from cryopreserved sperm or embryos, as well as cryopreservation and storage of sperm from existing lines.

SERVICES & CAPABILITIES

Primary Services Offered:

- Design and generate transgenic mouse models by using the Crispr Cas9 zygote injection
- Generation of transgenic mouse models via embryonic stem (ES) cell injection
- Sperm cryopreservation and storage
- Re-derivation of mouse strains from cryopreserved sperm or embryos
- Mouse embryos aggregation and blastomere biopsy

Technical Expertise Available:

Our team offers expert consultation and technical support for procedures including embryo and sperm collection, embryo transfer, fetus collection at various stages, tail vein injection and retro-orbital blood collection.

ACCESS INFORMATION

Who Can Access:

Our services are available to researchers within the University of Pennsylvania community, as well as to external collaborators.

How to Get Started:

Please contact us via e-mail (nleu@upenn.edu) with a brief description of the specific gene of interest and the desired genetic modification. We will follow up with a Zoom meeting to review the process and discuss next steps.

PRICING & FUNDING

The Penn internal rates are as follows:

- $3,000 for designing the constructs, genotyping of offsprings and sequencing the positive founders (optional but highly recommended).
- $3,000 for injecting the constructs into zygotes (includes donor and recipient mice, and cage costs up to the weaning age).
- $3,000 for ES-cell injection and generating chimeras.
- $3,000 for re-deriving mice from cryopreserved sperm.
- $800 for sperm cryopreservation (includes one year of storage).

For external investigators:

- The rate for each of the following services: construct design, zygote injection, and mouse re-derivation is $5,000.
- The fee for sperm cryopreservation is $1,300.

ABSTRACT NUMBERS

The abstract numbers below correspond to the poster board number.
Abstracts are ordered alphabetically by the presenting author's last name.

1. Seongjue Ahn
2. Loveleena K. Anand
3. Nasreen Bano
4. Akshaya Nidhi Bhati
5. Jerrianne Brandly
6. Quoc-Thang Bui
7. Elliot M. Bullen
8. Alyssa Chalmin Katz
9. Carly Ciociola
10. Arin Cox
11. Lindsay Daly
12. Mayura R. Dhamdhere
13. Thomas Ede
14. Layne Freeman
15. Erick Gagne
16. Elizabeth A. Greif
17. Laura Hutchins
18. Sarah Ibach
19. Lang Jiang
20. Bethany Keen
21. Robb Kessel
22. Scott L. Korte
23. Caitrin Lowndes
24. Caitrin Lowndes
25. Elizabeth J. Malozzi
26. James O. Marx
27. Anna M. Massie
28. Leif K. McGoldrick
29. Jaclyn R. Missanelli
30. Leonardo Murgiano
31. Veridiana Nadruz
32. Kevin D. Niedringhaus
33. Jessica K. Niggel
34. Sheridan A. O'Connor
35. Thomas D. Parsons
36. Thomas D. Parsons
37. Dhani Prakoso
38. Zachary Royle
39. Samara Schreier
40. Carlo Siracusa
41. Louise Southwood
42. Kei Takahashi
43. Eoin C. Whelan
44. Clara Wilson
45. Tiffany C. Wu
46. Yoshihiko Yu
47. Caroline Zagoren
48. Abigale H. Zoltick

POSTER ABSTRACTS

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

1. NATURAL VS EXPERIMENTAL CONTAMINATION OF EXTERNAL FIXATOR PINS IN A SHEEP MODEL.

Seongjue Ahn[1], Kaylee N. Philbrick[1], Samir Mehta[2], and Thomas P. Schaer[1].

[1]Department of Clinical Studies–New Bolton Center, School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA; [2]Department of Orthopaedic Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA.

Orthopedic-related infections (ORIs) are a leading cause of revision after implant placement, yet most preclinical models rely on supraphysiologic inocula and laboratory-adapted strains. We compared a naturally acquired pin-tract infection model with an iatrogenic *Staphylococcus aureus* inoculation model in sheep. Four healthy, 2-year-old castrated Dorset sheep underwent mid-shaft tibial osteotomy stabilized with a half-pin, monoplanar external fixator (two proximal, two distal pins) without perioperative antibiotics. Animals were assigned to Cohort 1 (natural infection; n = 2) or Cohort 2 (inoculated; n = 2). In Cohort 2, 0.2 mL *S. aureus* (2.5 × 106 CFU/mL) was instilled at each pin site at closure. Clinical monitoring included daily observation and twice-weekly composite pin-site scores (pain, swelling, heat, erythema); radiographs were obtained serially and graded blinded for cortical lucency and periosteal reaction. At prespecified endpoints (Cohort 2 at 4 weeks; Cohort 1 at 8 weeks), tissues were collected for microbiology, histology, and micro-CT. One Cohort-1 animal was euthanized at 2 weeks for frame failure. Across the remaining animals, both models produced features of septic pin-tract infection. Radiographic changes appeared earlier in Cohort 2 (~1 week), whereas Cohort 1 showed minimal early changes but exceeded Cohort-2 scores by 4–7 weeks. Postmortem examination revealed mucopurulent discharge and pin loosening, particularly at proximal sites with greater soft-tissue coverage. *S. aureus* was isolated from all infected sites; β-hemolytic colonies were present in all pins from Cohort 2 and 56% from Cohort 1, with mannitol-fermenting colonies in 38% and 68%, respectively. Natural infection emerged within ~30 days, about 19 days earlier than in our prior systemic-amikacin sheep cohort. Both approaches yielded clinically relevant infections; the natural-infection model may better reflect clinical reality and avoid supraphysiologic inocula, supporting future evaluation of anti-infective technologies.

Research Grant: U.S. Department of Defense DM220115–CDMRP Award

2. EXPRESSION OF TETRASPANIN CD9 IMPACTS FILOVIRUS EGRESS AND SPREAD.

Loveleena K. Anand[1], Olena Shtanko[2], and Ronald N. Harty[1].

[1]Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA; [2]Host-Pathogen Interactions, Texas Biomedical Research Institute, San Antonio, TX.

Filoviruses, including Ebola (EBOV) and Marburg (MARV) viruses, are zoonotic pathogens that cause severe hemorrhagic fever in humans with mortality rates reaching up to 90%. Filovirus egress and spread is driven by the viral matrix protein VP40 and regulated both positively and negatively by a growing number of specific host interactors. Here, we identify tetraspanin protein CD9, a membrane organizing and scaffolding protein, as playing a role in facilitating efficient egress of VP40 VLPs, as well as authentic EBOV and MARV. Indeed, we observed a significant decrease in egress of VLPs and live filoviruses from CD9-KO cells compared to that from WT cells. Moreover, exogenous expression of CD9 rescued budding of VP40 VLPs back to WT levels in CD9 knockdown cells. These findings identify tetraspanin CD9 as a positive regulator of filovirus egress, and thus is a potential new target for antiviral therapies.

3. DECODING B-CELL LINEAGE ALTERATIONS IN YY1 KNOCKOUT MICE THROUGH SINGLE-CELL AND 3D GENOMIC ANALYSIS.

Nasreen Bano, Sulagna Sanyal, Sarah Naiyer, Suchita Hodawadekar, and Michael L. Atchison.

Department of Biomedical Sciences, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA.

Yin Yang 1 (YY1) is a multifunctional transcription factor that regulates gene expression by recruiting chromatin remodelers, modifying histones, and facilitating long-range chromatin interactions between enhancers and promoters. In hematopoiesis, lineage commitment is tightly controlled by transcription factors, chromatin architecture, and epigenetic regulators. During normal development, pre-pro-B cells commit exclusively to the B-cell lineage at the pro-B cell stage. In this study, we investigated the role of YY1 in B-cell lineage commitment using a conditional knockout (KO) model in pro-B cells cultured on OP9-DL4 feeder cells providing Notch signaling. Loss of YY1 disrupted B-lineage specification and promoted the emergence of alternative lineages, including T cells, macrophages, dendritic cells, and monocytes. Single-cell chromatin accessibility profiling revealed increased accessibility at alternative lineage genes and decreased accessibility at B-lineage genes in YY1 KO pro-B cells compared to wild-type. Similarly, single-cell transcriptomic analysis showed elevated expression of alternative lineage genes alongside repression of B cell-specific genes. Chromatin loops, play critical roles in gene regulation by bringing distant regulatory elements (e.g., enhancers and promoters) together. Hi-C analyses demonstrated enhanced chromatin loop interactions at alternative lineage genes whereas reduced loops were found at B lineage genes in YY1 KO pro-B cells indicating significant alterations in 3D genome organization. Together, these findings establish YY1 as a critical regulator of chromatin accessibility and 3D genome architecture required for maintaining B-cell lineage commitment and repression of alternative fates.

4. DETERMINATION OF ACCURACY AND EFFICIENCY OF AUGMENTED REALITY-BASED SURGICAL NAVIGATION SYSTEM VISAR FOR BRAIN BIOPSY IN DOGS VIA FEEDBACK FROM INTERACTIVE CANINE BRAIN AVATAR.

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Collecting diagnostic brain biopsy samples in dogs is challenging due to the complexity of the procedures, the need for prolonged and repeated general anesthesia, the variability of skull morphology across breeds, and narrow safety corridors. Missed targets expose the patient to the risk of non-affected tissue damage, require repeated passes, further prolong anesthesia, and increase the likelihood of complications. Although the augmented reality (AR)-based surgical navigation system VisAR has received FDA clearance for spinal navigation in human surgery, its use in intracranial interventions in veterinary neurosurgery has not been studied. In this study, to assess feasibility, we combined VisAR with a computed tomography/magnetic resonance imaging (CT/MRI) visible canine brain phantom previously developed by our group, designed for anatomical fidelity and interactive feedback. Data from a dog diagnosed with glioma were used to create a patient-specific physical twin of the brain using PolyJet printing. A conductive tumor and a personalized biopsy probe provided audible confirmation upon contact with the target lesion. In a randomized, intra-individual crossover study, operators performed paired biopsy attempts to a 5-mm target under two conditions:

(1) using AR navigation with VisAR and (2) using an alternative neuronavigation system (Brainsight). Accuracy with VisAR was similar to that of the conventional neuronavigation system. However, the median operating time was significantly shorter with VisAR. Similarly, the learning curve with VisAR was significantly shorter than with Brainsight. First-pass confirmation was more frequent with VisAR in the group of less experienced neurosurgeons. On a canine, patient-specific 3D model, VisAR improved performance compared to the conventional approach by providing frameless navigation validated by independent feedback. These findings support rapid translation to cadaveric and clinical studies, with the potential to shorten anesthesia time, reduce the number of passes, limit risks to canine patients, lower costs, and improve diagnostic efficiency.

5. FLEX VENTILATION IMPROVES PULMONARY FUNCTION IN A RIB-TETHERED MINI-PIG MODEL OF THORACIC INSUFFICIENCY SYNDROME.

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Early-onset scoliosis is associated with significant morbidity due to its close link with thoracic insufficiency syndrome (TIS). This condition involves anatomical constriction of the thorax, which prevents uniform expansion, impairs lung inflation, and hampers lung growth. As a result, it leads to progressive respiratory and cardiovascular impairments. The aim of this work is to address these issues. This study aimed to investigate long-term changes in pulmonary function in a large animal model of TIS, and to evaluate whether Flow-controlled ventilation (FLEX) enhances pulmonary mechanics and ventilation-perfusion matching compared to conventional pressure ventilation (CPV). Under IACUC approval, rib tethering of the right hemithorax was performed in Yucatan mini-pigs (n=4) at 8 weeks of age to induce thoracic deformity. Two age- and weight-matched animals served as controls. Longitudinal imaging and pulmonary function assessments were conducted for 9 months (cohort 1) and 3 months (cohort 2). Digital radiographs and CT measured Cobb angle and mean lung volume (MLV). Tidal volume (TV) was recorded during spontaneous breathing. Under anesthesia, dynamic compliance (Cdyn), PaO_2/FiO_2 ratio, and dead space ($PETCO_2/PaCO_2$) were measured during CPV and FLEX.

In cohort 1, one tethered animal developed a 25° curvature. Compared to the control (MLV 1912 cm^3; TV 485 mL), the tethered animal had reduced MLV and TV (1586 cm^3; 290 mL). During CPV, Cdyn was lower (32 vs 55 mL/cmH_2O) but improved by 68% with FLEX. FLEX also increased PaO_2/FiO_2 (390→468 mmHg) and reduced dead space (18%→3%).

In cohort 2, tethered animals did not develop sustained curvature, but MLV and TV remained lower than controls (1051 cm^3, 158 mL vs 1420 cm^3, 223 mL). Cdyn was reduced during CPV (35 vs 47 mL/cmH_2O) and improved only in tethered animals with FLEX (45 mL/cmH_2O). Dead space fell from 12% to 4%.

These findings show that chest deformity impairs pulmonary function, and FLEX ventilation improves compliance and gas exchange. FLEX may help optimize respiratory function in children with thoracic deformities undergoing anesthesia or requiring long-term non-invasive support.

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6. ROLE OF SPTBN2 IN T CELLS WITHIN THE TUMOR MICROENVIRONMENT.

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Spectrin beta, non-erythrocytic 2 (SPTBN2), has been identified as a crucial factor that promotes tumor cell proliferation, invasion, and metastasis, while inhibiting apoptosis and ferroptosis, thereby contributing to tumor progression and a poor prognosis in several malignancies. Yet, its role in immunoregulation and the tumor microenvironment (TME) remains poorly understood.

We found that SPTBN2 expression was markedly increased in human T cells under conditions of nutrient deprivation *in vitro* and in tumor-infiltrating compared with splenic T cells *in vivo*. Transcriptomic analyses across pan-cancer datasets demonstrated that elevated SPTBN2 expression was inversely correlated with CD8A levels and intratumoral $CD8^+$ T cell infiltration, particularly in colorectal and pancreatic cancers, and was associated with poor patient survival. Using syngeneic tumor models, genetic deletion of *Sptbn2* in the TME enhanced intratumoral $CD8^+$ T cell activity, alleviated T cell exhaustion, slowed tumor growth, and improved responsiveness to chemotherapy.

Functional assays further revealed that *Sptbn2* deficiency in anti-hCD19 CAR-T cells increased IL-2 and IFN-γ production and augmented cytotoxicity against antigen-bearing cancer cells. Loss of *Sptbn2* also reduced trogocytosis between tumor and CAR-T cells while promoting CAR-T expansion *in vitro*. Moreover, *Sptbn2*$^{-/-}$ CAR-T cells exhibited superior tumor control compared with the wild-type (WT) controls against hCD19-expressing B16F10 tumors.

These findings suggest that SPTBN2 functions as an immunoregulatory factor that drives T cell dysfunction and constrains effective antitumor immunity. Targeting *Sptbn2* may therefore represent a promising strategy to enhance CAR-T cell function and improve clinical outcomes in solid tumors.

7. ESTABLISHMENT OF FODDER-BASED WORKING RIPARIAN BUFFERS WITHIN A ROTATIONAL GRAZING PROGRAM FOR DAIRY HEIFERS.

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Riparian buffers—plantings of trees and shrubs along streams—are a well-established conservation practice. However, farmers can be resistant to such buffers as they can take land out of production. "Working" riparian buffers aim to address this challenge by integrating economic outputs (fruit, nut, floral, or biomass crops) into buffer design. A recently established agroforestry study site at Penn Vet's New Bolton Center is investigating the potential to incorporate fodder for heifers into working riparian buffers—allowing cows to periodically coppice the shrub and have access to additional feed sources, particularly when grass regrowth might be limited. While more common in New Zealand's dairy industry, these fodder blocks are novel to southeastern Pennsylvania. In Spring 2024, 24 different fodder blocks were established to test combinations of species, stock type, planting method, and distance from the stream channel. Year-1 monitoring of the plants during the Summer of 2025 revealed a large variation in the survivability across the different blocks, ranging from 22% to 100%. A linear model was implemented in R to examine which factors contributed to fodder block survivability. Within 125 feet of the stream channel, all factors except plant species had no significant impact on survivability. However, the willow cultivar Streamco had 3-fold less mortality compared to the native willow stock as well as other shrub varieties ($p<0.001$). Notably, native dogwoods and hazelnuts averaged below target survival,

suggesting they may require additional support or be better suited for other contexts. Further analysis of biomass production will support a more complete picture of forage availability in the blocks. Cows will begin grazing the fodder blocks in Summer 2026, providing additional insights into animal behavior, forage value, and ecological impacts. The study is part of a larger interdisciplinary agroforestry project at New Bolton Center that aims to better understand interactions between agriculture and the natural world.

8. EFFICACY AND IMMUNOGENICITY OF A TRIVALENT HSV-2 GC2, GD2, GE2 NUCLEOSIDE-MODIFIED MRNA VACCINE AGAINST HSV-1 EYE INFECTION IN MICE.

Alyssa Chalmin Katz, Kevin Egan, Zauraiz Syeda, Sarah Son, Bahiyah Watson, Enrico Radaelli, Charles-Antoine Assenmacher, Manaswini Gopalakrishnan, Valerie Bromberg, Sita Awasthi, Gary H. Cohen, and Harvey M. Friedman.

Ocular infection with herpes simplex virus type 1 (HSV-1) can lead to herpetic keratitis, a leading cause of corneal blindness in the US and other developed countries. Our lab is working on a vaccine to prevent genital herpes. The vaccine consists of nucleoside-modified mRNA in lipid nanoparticles (LNPs) that express herpes simplex virus type 2 (HSV-2) glycoprotein gD2, an entry molecule, and two immune evasion molecules, glycoprotein C (gC2) that inhibits complement, and glycoprotein E (gE2) that blocks activities mediated by the IgG Fc domain. To evaluate whether the HSV-2 trivalent vaccine protects against ocular HSV-1 infection, 9-10 mice per group were immunized IM twice separated by 1 month with PBS (controls), 1 ug, or 10 ug (total dose) of the vaccine, and infected 1 month later topically on the cornea with 10^6 plaque-forming units ($10*LD_{50}$) of HSV-1 McKrae strain. Animals were assessed for survival, ocular disease, neurologic signs, and weight loss for 14 days post-infection. Serum was collected pre-infection for IgG ELISA and neutralizing antibodies, and tissues were harvested at euthanasia for measurement of HSV-1 titers by viral cultures and qPCR. 10 additional animals were similarly immunized with either PBS (n=5) or 10 ug (n=5), infected, and sacrificed at day 5 post-infection. Both vaccine doses protected mice equally well. All 19 animals in the vaccine groups survived compared with 4/10 (40%) in the PBS group (p=0.0108, two-tailed Fisher's exact test). 11/15 (73.3%) animals in the vaccine groups were completely protected against eye disease, compared to 2/10 (20%) in the PBS group (p=0.0045). Across all animals that received the 10 ug vaccine, 13 of 15 showed no detectable HSV-1 PFUs or HSV-1 DNA in the eye, trigeminal ganglion, cerebrum and cerebellum, brainstem, and olfactory bulb at acute (day 5 post-infection, n=5/tissue) or chronic (day 49-52 post-infection, n=10/tissue) timepoints, compared to 5 of 15 control animals (p=0.0078). Serum IgG ELISA against HSV-1 gC1, gD1, and gE1 and neutralizing antibody titers showed that the HSV-2 vaccine produced cross-reactive antibodies against the HSV-1 homologs. The HSV-2 trivalent mRNA vaccine is a promising candidate for preventing HSV-1 infection of the eye through primary infection of the cornea.

9. APPLICATION OF AN ELECTRIC CURRENT IN THE DEVELOPING CHICKEN EMBRYO INDUCES SPINAL DEFORMITY.

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Congenital scoliosis affects 1 in 1000 live births. The risk of spine deformity progression depends on various factors, including morphology, anatomical location, and rate of spine growth. Given that little is known about the pathophysiology of congenital spine deformity, clinicians are unable to make informed treatment decisions. The purpose of this study is to examine the effects of applying targeted electric current on the formation and location of congenital spinal deformities in the developing chicken embryo.

47 specific pathogen-free (SPF) eggs were incubated until embryonic day 3 (E3) when the shell was windowed for intervention. In the intervention group (n=42), an electrical current was delivered through electrodes placed above (n=11), below (n=12), and at an oblique angle to the vitelline vessels (n=19). Five eggs served as controls. Eggs were sealed and incubated until E10, then the embryos were sacrificed. At E17, 11 eggs were assessed using μCT. For histological analysis, select specimens harvested at E10/E11 were sectioned and stained to observe morphological defects of the vertebrae.

The electroporation protocol resulted in high survival (n=33/46, 72%) and high spinal deformity (n=29/33, 88%) rates. Spinal defects (n=30/33, 90%) were region-specific. All control embryos survived (5/5) without spine deformity (0/5), highlighting the significant difference in deformity rates between groups ($p<0.0001$). μCT assessment identified unsegmented bars and block vertebrae at the thoracolumbar region. In scoliotic chicks, bilateral defects were observed in 4/9 specimens with fusion, and unilateral defects were observed in 5/9 specimens with fusion. Histological evaluation of specific regions in representative specimens confirmed segmentation defects, not present in controls.

The extent and location of vertebral fusion can be explained by the location and severity of the vascular lesion (6), which could be controlled through targeted electrode placement. We suggest that vascular injury is the mechanism inducing vertebral segmentation defects in this chick model.

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10. TECHNIQUES TO STUDY CHIMERISM AT THE TISSUE LEVEL IN HUMANIZED MICE.

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Understanding the origin, distribution, and biology of different cell populations in chimeric mice is critical for interpreting the pathological changes developed in these models. To this aim, the methodological work presented here illustrates the validation and application of a collection of labeling techniques to differentiate between specific mouse and human tissue/cell components in formalin-fixed paraffin-embedded samples from chimeric mice, especially those bearing human tumor and immune cells. First, broad approaches to identify cells of human origin using ubiquitous immunohistochemical targets such as HLA-A, Ku80, and human mitochondrial 60kDa protein (hMito) were established using specimens from humanized mice and a human tissue microarray including both normal and neoplastic samples. Due to its crisp membranous immunoreactivity, HLA-A was the most useful marker for visual human cell identification; however, Ku80 and hMito may be suitable options when HLA-A is not expressed in the cells of interest. Importantly, using one or more of these markers provides a broad range of coverage for the vast majority of human-derived cells in chimeric mice. Second, tailored immunohistochemical or *in situ* hybridization methodologies to distinguish specific human or mouse cell subsets are presented, focusing on immune/inflammatory cells and human CAR T-cells. These diverse approaches are accompanied by descriptions of case examples highlighting practical diagnostic and experimental applications in the context of various humanized mouse models. While not comprehensive, this work represents a valuable starting reference for pathologists and investigators working with humanized mouse models and seeking to add spatial resolution to the complex landscape of chimeric tissues.

11. COMPARISON OF VOCALIZATIONS OF SOWS FOLLOWING NEEDLESS INTRADERMAL AND CONVENTIONAL INTRAMUSCULAR VACCINATION.

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Use of intradermal (ID) vaccination in pigs is less time consuming and labor-intensive compared to conventional intramuscular (IM) vaccination and does not compromise safety or efficacy. When adopting new technologies, it is important to consider their impact on the wellbeing of the animals and animal caretakers. Assessing vocalizations following vaccination may provide insight into a pig's affective state. The objective of this study was to determine if the vocalizations differ between sows vaccinated intradermally and intramuscularly. Over the course of 15 weeks, sows (n = 104) were blocked by parity and randomly allotted into ID (n = 50) and IM (n = 54) treatment groups. Sows were recorded for two minutes following vaccination and the videos were coded for types of vocalizations (bark, long grunt, squeal, scream, no vocalization) differentiated by pitch and duration of vocalization. Sound intensity readings were performed at the time of vaccination using a sound level meter. Intramuscularly vaccinated sows were more likely to vocalize (OR = 2.9 Cl 1.0 to 8.8) and vocalized more times (p = .0001), making 1.5 ± 1.1 vocalizations compared to 0.68 ± 0.79 vocalizations made by the ID vaccinated sows. Intramuscularly vaccinated sows were more likely to squeal (OR =

11.0 CI 2.3 to 102) and bark (OR = 2.4 CI 1.0 to 5.8). There was no difference (p = .43) in the max decibel recorded during vaccination between the ID (78.8 ± 8.0) and IM (77.4 ± 7.3) groups. Overall, decreased vocal reactions to ID vaccination suggest that ID vaccination may improve animal welfare and reduce vaccinator noise exposure.

12. DAMAGE INDUCED CANCER CELL MEDIATED-TROGOCYTOSIS SUPPRESSES CD8+ CYTOTOXIC T CELLS, CONTRIBUTING TO IMMUNOSUPPRESSION IN THE TME.

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Cancer cells can inactivate cytotoxic T lymphocytes (CTLs) in the tumor microenvironment (TME), through a number of mechanisms including trogocytosis, a process where CTLs acquire material from tumor cells at immune synapses leading to their inactivation. The mechanisms governing this process, however, are not fully understood. Here, we establish a novel form of trogocytosis, that is triggered by stress-inducing factors within the TME and is independent of tumor-associated antigen recognition. We identify the Phosphatidylserine (PS)-Tim3 signaling axis as a key regulator of both non-canonical and antigen-stimulated trogocytosis between cancer cells and CTLs. In response to TME or therapeutic stress, live, non-dying cancer cells reversibly externalize PS, a lipid predominantly located on the inner membrane, via the activation of scramblases. This externalized PS on cancer cell surface interacts with the Tim3 receptor on CTLs, leading to the transfer of PS lipid molecules onto CTLs. This transfer is associated with T-cell exhaustion, marked by reduced proliferation (Ki-67) and cytolytic molecule expression (e.g., perforin, Granzyme-B, IFN-γ), suppressed cytotoxic activity, and increased expression of exhaustion markers (e.g., PD1, Lag3, TOX, CTLA4). Importantly, inhibition of scramblases or externalized PS in cancer cells, or blocking Tim3 on CTLs reduces biomolecule transfer onto CTLs. Our findings reveal that disrupting PS-Tim3 signaling pathway could be a promising strategy to inhibit cancer cell-CTL trogocytosis and potentially enhance the efficacy of T-cell-based immunotherapies for solid tumors.

13. GILTS ARE MOTIVATED TO EXIT A STALL.

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Stalls (or crates) are still a common type of housing in the swine industry, despite public concern and regional legislation restricting their use. In this study, we examined the motivation of gilts to exit a stall. Sixteen stall-naïve gilts (Large White x Landrace) were locked for 60 min in a gestation crate that had been mounted with a novel apparatus allowing continuous monitoring (2 Hz measuring frequency) of the force applied to its back gate by the animal. Raw force measurements were low-pass filtered and discrete pushing events identified via local maxima. All gilts displayed some level of motivation to exit the crate, ranging from 41 to 173 in the number of pushing events, as well as exerting a maximum force applied from 124 N to 645 N. A hierarchical cluster analysis applied to the median and interquartile range (IQR) of force generated during individual pushing events yielded two behavioral profiles. One group of eight animals was more active than the other. This group exhibited a greater number of pushes, recorded a higher maximum, median force and its IQR, as well as a shorter time interval between two pushes (all t-tests with a $P < 0.05$). While all

these naïve animals worked to leave the stall, gilts displayed different motivation profiles in trying to exit the stall consistent with a reactive/proactive framework. Taken together these findings provide further evidence to support stall confinement as aversive to swine but highlight the complexities in understanding and improving pig welfare.

14. EARLY ONSET OF ALPHA MANNOSIDOSIS CLINICAL SIGNS IN A 6-WEEK-OLD KITTEN.

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A 6-week-old domestic shorthair male kitten was reported for lethargy and abnormal behavior compared to his littermates. The kitten had a confirmed diagnosis of alpha-mannosidosis, a lysosomal storage disease that eventually leads to multisystemic clinical signs involving the nervous, cardiac, hepatic, and skeletal systems. Notably, this kitten had received three adeno-associated virus (AAV) vector gene therapy treatments via carotid artery on 11/25/25, 11/27/25, and 11/29/25. Clinical signs were reported on 11/30/25. On physical examination, the kitten displayed generalized tremors, focal twitching of the eyes and muzzle, loss of conscious proprioception, and a markedly distended yet easily expressible bladder. Due to an insufficient blood sample volume, an i-STAT analysis could not be performed; however, a glucometer reading confirmed normoglycemia. Given the severity of the clinical signs and the poor long-term prognosis, humane euthanasia was elected. Gross necropsy findings revealed a markedly distended urinary bladder. Histopathological evaluation revealed severe, diffuse cytoplasmic vacuolation of neurons within the spinal cord, dorsal root ganglion, cerebrum, cerebellum, and urinary bladder. Additionally, marked cytoplasmic vacuolation was observed in the liver, spleen, and lungs. These findings were consistent with a diagnosis of alpha-mannosidosis and represent the earliest and most severe clinical manifestation of the disease documented in a kitten of this age. To date, clinical signs of this magnitude have not been reported prior to 12 weeks of age.

15. ACCESSING NATURE: ENGAGING COMMUNITIES IN URBAN WILDLIFE RESEARCH ACROSS PHILADELPHIA.

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By 2050, nearly 70% of the global population will live in cities. Though cities are built for people, wild animals also inhabit them, making it increasingly urgent to understand how urbanization shapes biodiversity and human–wildlife interactions. The Accessing Urban Nature Initiative establishes a trail camera network across Philadelphia in partnership with the Urban Wildlife Information Network (UWIN), local schools, nonprofits, and Penn institutions. Approximately 30 motion-triggered cameras will be deployed along a gradient of urbanization, seasonally (July, October, January, April). Images will be integrated into the UWIN database, enabling both local investigations and global analyses of urban ecology. This design creates opportunities to study species diversity, activity patterns, and behavioral adaptations to urban environments, while also allowing cross-city analyses of how climate change and land use influence wildlife.

The project will also examine links between biodiversity, social inequities, and access to urban nature—positioning Philadelphia as a case study for understanding coupled human–natural systems. Community science platforms such as WildTrax will engage volunteers and students in image classification, generating large-scale datasets while fostering broad participation in research. The Accessing Nature initiative aligns strongly with several key priorities outlined in Penn's *In Principle and Practice,* including addressing pressing global challenges related to biodiversity and climate change, engagement in data-driven research and applications, and strengthening connections between Penn and its neighbors, both locally and globally.

Research Grant: Draw Down the Lightning grant, Office of the President, University of Pennsylvania

Student Support: Stipends for two Penn undergraduate students

16. NOVEL SELENOP MISSENSE MUTATION IDENTIFIED IN CANINE MODEL OF POLYMICROGYRIA.

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Polymicrogyria (PMG) is one of the most common cortical brain malformations in people and also occurs naturally in dogs. The disease is characterized by an abnormal number of small gyri, the ridged structures on the brain's surface. Affected dogs can vary in presentation but often includes severe vision impairment and neurological deficits. Most reported cases to date are from a single breed, Standard Poodles, suggesting a breed-specific genetic predisposition. We performed genome-wide association studies for PMG using imputed low-pass sequencing data from 5 case and 85 unrelated control Standard Poodles. We identified multiple novel loci associated with the disease, where the most prominent peak exhibited a *p*-value more than 10^{12}-fold lower than other signals. Additional allele frequency analyses using a database of high-coverage whole genome sequences from 3,023 dogs further validated this region, and 197 candidate variants unique to cases but rare in non-poodle breeds were identified. All candidate variants were evaluated using various *in silico* programs. Only one variant was a missense mutation, which was predicted to be deleterious (Polyphen-2 score = 0.625) and harbors a substituted residue that is absent at this site in orthologous proteins across other species. The mutation occurs in exon 5 of *SELENOP,* a gene encoding selonoprotein P, which is crucial for selenium transport in the body and for normal brain development and function. In people, dysfunction across selenoproteins has been linked to developmental and degenerative diseases, while in dogs, another mutation within *SELENOP* itself was associated with cerebellar ataxia. Further investigation of the variant is warranted, and Sanger sequencing to determine its impact on disease within the breed is underway.

Research Grant: Van Sloun Fund for Canine Genetic Research; Foundation Fighting Blindness; NEI/NIH EY 006855

17. ELUCIDATING MECHANISMS OF COOPERATIVE IMMUNITY IN INFLUENZA INFECTION.

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Influenza infection is a yearly threat to human health resulting in tens of thousands of deaths per season in the United States alone. Seasonal vaccines that elicit neutralizing antibodies to circulating strains of flu are widely used, but, there are inherent limitations to this vaccine strategy. The neutralizing antibodies must target surface proteins hemagglutinin and neuraminidase to coat and halt the virus in its tracks; however, these surface proteins are highly prone to mutation, and even a single amino acid mutation can render neutralizing antibodies useless. Conversely, CD8 T cells can recognize internal conserved flu proteins, such as nucleoprotein, and kill flu-infected cells, providing viral clearance and broad protective immunity. An underappreciated collaboration exists between CD8 T cells and non-neutralizing antibodies in the context of influenza where, in combination, these two seemingly disparate branches of the immune system lead to decreased weight loss and mortality from H1N1 infection in mice, a phenomenon termed cooperativity immunity. Cooperativity immunity is dependent on Fc receptors and lung phagocytes, but further mechanistic details are not understood. Here, we have developed an experimental system to elucidate the antibody- and cell-dependent mechanisms underlying cooperative immunity to influenza disease. In our experimental model, we vaccinate mice with an mRNA vaccine to induce nucleoprotein-specific CD8 T cells and then inject mice with anti-nucleoprotein, non-neutralizing monoclonal antibodies one day prior to influenza challenge with the H1N1 strain PR8. We demonstrate that vaccination alone induces immune pathological CD8 T cells while the addition of non-neutralizing antibodies alleviates this exacerbated disease and mediates disease protection. Using this model, we will alter the antibody properties (antigen specificity, Fc domain subtype) and CD8 T cell effector functions that drive cooperative immunity and explore broad immunity against diverse influenza strains, including H3N2, H5N1, and influenza B.

18. ANTICIPATORY BEHAVIOR PRIOR TO FEED DELIVERY OF POST-WEANED SOWS.

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The impact of stall confinement on the emotional health of post-weaned sows is poorly understood despite being an integral component of their welfare. A possible method for gauging emotional welfare is through measuring anticipatory behavior (AB), an increase in activity that occurs in the appetitive phase prior to receiving a known reward. This indicator of reward sensitivity is thought to be influenced by an animal's underlying emotional state and may therefore provide insight into their current affective state. Thus, we investigated how two housing treatments impacted AB in response to the signaling of feed delivery. Sows (n = 24) were randomly assigned to housing in either an individual pen (14 ft^2) or a standard gestation stall (44 ft^2) immediately post-weaning for seven days. Twice daily, 15 minutes before the scheduled delivery of feed at 8 AM and 1 PM, behavior was video recorded. Pen-housed sows were moved into stalls adjacent to the stall-housed sows before each recording session to ensure standardized conditions for the

observation of AB. AB was measured continuously prior to feed delivery using an ethogram assessing posture, activity, head location, and snout placement, and defined as the total number of behavioral transitions during the 15-minute anticipation period. The overall impact of housing on AB was investigated via the total number of behavioral transitions, and the kinetics of AB were studied through the cumulative number of behavioral transitions performed per minute. Contrary to our expectations, there was no effect of housing on AB; however, we found significant impacts from time of day ($p < 0.001$) and individual animal ($p < 0.001$). These observations support the relevance of our AB measure as the sows appear to anticipate feeding more in the morning after a longer wait between feedings (~5 vs ~19 h). A 5-fold difference was observed between animals across the study, as behavioral transitions/min ranged from 6.73 to 35.33. These results lay vital groundwork for the implementation of reward appraisal-based methods such as AB for assessing post-weaned sow welfare and further emphasize the importance of individual animal variation and type of reward in the assessment of emotional states.

19. INCREASED CCR4 EXPRESSION IS ASSOCIATED WITH POOR OUTCOMES IN CANINE RENAL CELL CARCINOMA BUT NOT IN HISTIOCYTIC SARCOMA.

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The composition of the tumor microenvironment (TME) is implicated in the progression and prognosis of multiple malignancies in human and canine patients. Classically increased numbers of anti-tumor effector T cells have been associated with favorable patient outcomes, whereas increased densities of immunosuppressive cells such as regulatory T cells (Tregs) are associated with poor outcomes. Chemokine receptors including the C-C chemokine receptor 4 (CCR4) help orchestrate the migration of immune cells within the TME and CCR4 is highly expressed in immunosuppressive Tregs. However, CCR4 can be expressed by other immune subsets and by malignant renal cell carcinoma (RCC) cells in humans. In this study we quantified the number of CCR4+ cells in canine RCCs that were sparsely infiltrated by T cells (immunologically "cold") and compared this to CCR4 expression in canine histiocytic sarcomas that were relatively heavily inflamed with T cells (immunologically "hot"). We found a spectrum of CCR4+ cell numbers in both tumor types. Whilst there was no significant difference between the density of CCR4+ cells between canine RCC and HS, increased numbers of CCR4+ cells were significantly associated with worse outcomes in canine RCC but not in HS. As CCR4+ cells can be therapeutically targeted by monoclonal antibodies in the veterinary clinic our study provides impetus for further investigation of CCR4 in canine RCC. Future research to determine which cells express CCR4 in the TME as well as the biologic role of CCR4 in canine RCC could provide further rationale toward therapeutically targeting this receptor.

20. DETECTING BISPHOSPHONATE USE IN EQUINE ATHLETES THROUGH AN UNTARGETED METABOLOMICS AND LIPIDOMICS APPROACH.

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Bisphosphonates are approved by the US Food and Drug Administration in horses older than 4 years of age and are of concern to the equine racing community due to their ability to provide analgesia while inhibiting the breakdown of bone by osteoclasts. They are highly polar and have poor ionizability thus making them difficult to detect with mass spectrometry and requiring extensive sample preparation. Therefore, an alternative approach using untargeted metabolomics and lipidomics was performed to identify potential biomarkers associated with the administration of bisphosphonates within equine athletes. An eight-horse case-control OsPhos® administration study was conducted over a 12-week period. Six metabolomics and lipidomics workflows were implemented to analyze the plasma samples, in a randomized manner, for optimal metabolome coverage. Compound Discoverer was used to detect and identify features using metabolomics and lipidomics algorithms and library searching, such as mzCloud, ChemSpider, BioCyc, the Human Metabolome Database and the Kyoto Encyclopedia of Genes and Genomes.

Metaboanalyst 6.0 was used to visualize the data and identify statistically significant biomarkers. Compound Discoverer was able to reduce the many features within the six workflows to those which were actual peaks. Data transformation reduced bias within the data, allowing for the discovery of significant biomarkers. These biomarkers that experience a smaller fold change may go undetected without transformation due to the impact from biomarkers skewing the data. Four of the six workflows achieved separation between control and treated horses with good accuracy and predictability through orthogonal partial least squares-discriminant analysis models. Potential biomarkers were identified using a fold-change cut off greater than 2.0, a p-value of less than 0.05 and a Variable Importance in Projection score greater than 1. A resulting 124 potential biomarkers were established from five of the six workflows for further investigation using a second independent set of horses in the OsPhos® administration study.

Research Grant: Racing and Medication Testing Consortium

21. CT/MRI-VISIBLE CANINE BRAIN AVATAR FOR NEUROSURGICAL TRAINING AND BIOPSY PLANNING.

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Advancements in 3D printing technology have propelled its utility in human and veterinary medicine for teaching, surgical planning, and procedural practice. Complex clinical workflows and a lack of realistic training models have prevented widespread clinical implementation of intracranial interventions in veterinary medicine. Currently, many phantoms produced for medical settings are limited in their anatomical representations or compatible imaging

modalities. Computer-aided design bridges the gap between a patient's imaging data, segmenting individual regions of interest, and selecting materials to produce the same imaging features. Digital Anatomy printers with PolyJet systems allow for the use of multiple materials to accomplish these designs and produce a usable patient-specific physical avatar that behaves like the original patient. This study provides a ready-to-use guideline and workflow system of utilizing the Digital Anatomy printer to develop a physical canine brain avatar based on a specific patient's imaging data that accurately depicts patient-specific anatomy in CT and MRI scans, which can ultimately be used for next-generation procedural planning and practice. Tissues of interest were segmented, and printing materials were selected to mimic the desired imaging properties. Avatars were produced using a 3D PolyJet system and underwent CT and MRI scans for evaluation. Avatar material intensity/Hounsfield Units, dimensions, and selected biopsy track were directly compared to the patient data for similarity. Our avatars showed the desired signal in both CT and MRI, with similar proportional material and tissue intensities across the imaging spectrum and minimal dimensional variation between the avatars and the patient. This study established guidelines for canine brain avatar manufacture with DAP and validated the workflow of converting patient-specific clinical imaging to a 3D printed avatar that is anatomically accurate and visible in CT and MRI, producing a unique model for clinicians.

22. NOVEL METHOD FOR PRESERVATION OF POLY-CAPROLACTONE SCAFFOLDS IN FFPE HISTOLOGY.

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Osteoarthritis (OA) is an orthopedic condition that induces chronic degeneration in tissues of the joint in more than 600 million people worldwide. Despite its high prevalence, treatment options for this condition are not yet ideal for patients. To overcome the challenges that current treatment with total joint replacements or early surgical intervention provides, the field has turned towards novel biomaterials as a solution. The use of biodegradable scaffolds composed of substances such as polycaprolactone (PCL) to support osteochondral repair has been widely investigated in recent years. However, evaluation of these implants by traditional histological methods after *in vivo* studies is impacted by PCL's low melting point of 60°C and ready degradation in Xylenes. As a result, histology examining PCL-implanted tissue often is only able to show small fragments of scaffold remaining within the tissue. This inability to visualize PCL on traditional Formalin-Fixed Paraffin Embedded (FFPE) histology sections limits the ability of researchers to examine the interactions that PCL and newly formed tissues may have on the cellular level. To address this, we developed a novel tissue processing protocol that sought to both preserve the integrity of PCL implants in high-quality FFPE sections while also reducing processing time. We hypothesized that combining the use of low-melting-temperature paraffin wax, d-limonene clearing agents, and warm tissue infiltration would enable visualization of PCL on FFPE histology sections with minimal impact to tissue quality. Histological results indicate that this novel processing protocol preserved PCL implant material while reducing manual processing times compared to previously reported protocols. In addition, results show protocol provides simultaneous evaluation of both implant and regenerated tissue within the same slides. These findings underscore the efficacy of our protocol in the evaluation of osteochondral tissue implants and provide a strong foundation for further study in the field of biomaterial research.

23. A RANDOMIZED, PLACEBO-CONTROLLED CROSSOVER STUDY OF BEXAGLIFLOZIN TREATMENT IN HORSES WITH NATURALLY-OCCURRING INSULIN DYSREGULATION.

Caitrin Lowndes, Daniela Luethy, Darko Stefanovski, Georgia Skelton, Jeaneen Kulp, and Andrew van Eps.

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A bexagliflozin formulation registered for cats could be effective for treating insulin dysregulation (ID) in horses. We hypothesized that the sodium-glucose cotransporter 2 inhibitor bexagliflozin would reduce the insulin response to oral sugar tests (OST) in horses with ID.

Ten client-owned Arabian horses (5-18 years; 442-571 kg) with naturally-occurring ID (mean OST maximal insulin 88 [range 51-157]μIU/ml) were included in a randomized, blinded, placebo-controlled crossover: 5 horses received placebo and 5 received 15 mg bexagliflozin once daily (~0.03 mg/kg; BEXA3) for 10 days. After a 4 day washout, treatments (swapped) were continued for 10 days followed by a 12 day washout. Then, all horses were treated with 30 mg bexagliflozin (~0.06 mg/kg; BEXA6) daily for 7 days. An OST (0.15 ml/kg Karo syrup) was performed at the beginning and end of each treatment period. Insulin (resting and OST) and triglycerides were compared (pre- vs post-treatment) using a mixed-effects linear regression model.

Bexagliflozin treatment was associated with a mean [95% confidence interval] reduction in resting insulin (BEXA3: -15[-29 to -1.4]μIU/ml; BEXA6: -21[-35 to -6.5]μIU/ml); OST maximal insulin (BEXA3: -30[-51 to -8.8]μIU/ml; BEXA6: -46[-68 to -24] μIU/ml) and OST insulin area-under-the-curve (BEXA3 -2562[-4493 to -631]]μIU/ml*min; BEXA6 -4154[-6168 to -2139]] μIU/ml*min); P<0.001. Resting serum triglycerides slightly increased with BEXA3 (40[31-49]mg/dl) and BEXA6 (52[43-61] mg/dl) compared to no treatment (32[25-38]mg/dl); P<0.001. No significant changes were associated with placebo (P>0.05).

In this cohort, short-term oral bexagliflozin treatment was effective for insulin control with only minor increases in serum triglycerides.

Research Grant: Laminitis Research Fund, University of Pennsylvania

24. DECREASED SERUM ADIPONECTIN AND INCREASED LEPTIN/ADIPONECTIN RATIO ARE ASSOCIATED WITH INSULIN DYSREGULATION AND PRE-EXISTING LAMINITIS IN LIGHT BREED HORSES.

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Associations between hypoadiponectinemia, insulin dysregulation (ID) and laminitis risk have been established in ponies, but not horses. Leptin/adiponectin ratio (L/A) is a potentially useful marker of ID and laminitis risk. We hypothesized that light breed horses with ID and/or pre-existing laminitis would have lower serum total adiponectin and increased L/A compared to healthy horses.

691 client- and university-owned mixed light breed horses were included in a cross-sectional cohort study. Resting serum total adiponectin, leptin and insulin concentrations (unfasted) were measured in all horses. Oral sugar tests (OST, 0.15ml/kg Karo syrup; n=328) and forefoot radiographs (n=214) were performed in a subset. Adiponectin, leptin and L/A were compared between horses with ID (resting or OST insulin >30μIU/ml; n=527) and non-ID horses (OST insulin <30μIU/ml; n=164); and laminitic (>2° radiographic distal phalangeal rotation; n=121) vs non-laminitic horses (n=93) using Mann-Whitney tests.

Median [interquartile range] serum total adiponectin (μg/ml) was lower (p<0.001) in horses with ID (6.1 [4.5-8.6) vs non-ID (8.3 [6.4-10.2]) and in laminitic (6.2 [4.7-8.5]) vs non-laminitic (8.0 [6.4-10.0]) horses. Leptin (ng/ml) was higher (p<0.001) in ID (11.5 [7.0-15.4]) vs non-ID horses (6.1 [4.4-8.9]), but was not different between laminitic (10.1 [5.9-15.6]) and non-laminitic horses (8.3 [4.9-13.0]); p=0.44. L/A ratio was higher (p<0.001) in horses with ID (2.1 [1.3-3.5]) vs non-ID (1.0 [0.6-2.7]) and in laminitic (1.8 [0.9-2.8]) vs non-laminitic (0.9 [0.6-1.8]) horses.

Resting adiponectin and L/A ratio are potentially useful markers of metabolic health in light breed horses. Associations between adiponectin and laminitis warrant further investigation.

Research Grant: Raker-Tulleners Endowment Fund and the Laminitis Research Fund of the University of Pennsylvania

25. QUANTIFICATION AND CONFIRMATION OF TRANEXAMIC ACID IN EQUINE PLASMA BY LC-MS/MS.

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Tranexamic acid is an antifibrinolytic drug that is used to treat bleeding disorders in horses. This compound is listed as Drug Class 4 according to the Association of Racing Commissioners International (ARCI). A method to confirm and quantify tranexamic acid in racehorses was developed and validated to ensure identification of the use of this compound and maintain the integrity of the sport. Tranexamic acid was recovered from equine plasma by protein precipitation using 0.1% formic acid in acetonitrile. The internal standard used was tranexamic acid $^{13}C_2{}^{15}N$. Tranexamic acid was detected on a Sciex 7500 triple quadrupole mass spectrometer by multiple reaction monitoring (MRM) using positive electrospray ionization mode. The analysis utilized a Hypersil Gold (100x2.1 mm) column with 0.1% formic acid in water and 0.1% formic acid in methanol as the mobile phases. The total analysis time was 5 minutes. The method was validated for extraction recovery, matrix effect, specificity, sensitivity, linearity, and inter- and intra-day accuracy/precision. Tranexamic acid was detected as a protonated ion $[M+H]^+$ with m/z of 158. The qualifying diagnostic product ions were m/z 95, 67, 123, and m/z 95 was used for quantification. The linear dynamic range of the method was 5 ng/mL – 200 ng/mL with a weighting factor of $1/x^2$. No interferences were detected at the retention time of tranexamic acid in six separate lots of blank equine plasma. Additionally, no carryover or significant matrix effect was observed. The extraction recovery of the method was found to be greater than 90%. The limit of detection was established to be 1 ng/mL, while the limit of quantification was determined to be 5 ng/mL. The inter- and intra-day accuracy of the method was determined to be within 90.6%–107%, and the precision was between 0.7%–10.4% for all quality control levels. Confirmation criteria are consistent with the Association of Official Racing Chemist recommendations. This method was successfully applied in equine doping control analysis to confirm tranexamic acid in a post-race horse plasma sample.

26. ANESTHESIA OF NEONATAL MICE USING ISOFLURANE AND HYPOTHERMIA.

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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.

27. NEAR-INFRARED IMAGING USING A CATHEPSIN-TARGETED, QUENCHED ACTIVITY-BASED PROBE IDENTIFIES NATURALLY OCCURRING CANINE APPENDICULAR OSTEOSARCOMA.

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Osteosarcoma is the most common primary malignancy of the skeleton. Despite advances in imaging modalities, neoadjuvant and adjuvant chemotherapy, and limb-sparing surgery over the past decades, there has been a general lack of improvement in patient survival rates. Tumor recurrence and metastases are associated with a worse prognosis, and complete tumor excision is critical for survival. The use of real-time intraoperative imaging to identify the extent of neoplastic disease facilitates the acquisition of tumor-free surgical margins while minimizing the morbidity associated with over-estimation of a tumor site. Spontaneous osteosarcoma in dogs is an established translational model of human osteosarcoma.

In this study, twelve dogs with spontaneous appendicular osteosarcoma received a cathepsin-targeted quenched activity-based probe (VGT-309) intravenously 16-20 hours before surgical amputation of the affected limb. The limb was imaged at 4 levels of dissection, and the tumor margins visible on near-infrared imaging were marked for comparison with histopathology and preoperative magnetic resonance imaging.

All appendicular tumors had visible fluorescence on cross-section of the bone, and the extent of this fluorescence coincided with MRI and histopathologic margins, with some variability associated with necrosis. All tumors had visible fluorescence through cortical bone, and all but one had fluorescence visible through soft tissues upon surgical approach to the limb.

This data supports the safety and feasibility of VGT-309 as a tool for evaluating the tissue extent of canine osteosarcoma and the investigation of this probe for intra-operative detection of osteosarcoma during limb-sparing surgery in humans.

Research Grant: This study was supported by the University of Pennsylvania School of Veterinary Medicine Companion Animal Research Fund (CARF) and a private donation (The Knott Family Foundation). The histopathology samples were processed by the University of Pennsylvania Penn Vet Comparative Pathology Core Facility (RRID:SCR_022438), which is partially supported by the Abramson Cancer Center Support Grant (P30 CA016520).

28. A HEADSPACE GC-MS/MS METHODOLOGY FOR THE DETECTION OF OXYGEN-CARRYING PFAS IN EQUINE SERUM.

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Per- and poly-fluoroalkyl substances (PFAS) are a class of compounds with beneficial uses, harmful effects, variable structures, and multiple other characteristics. Although the general conversation concerning PFAS is in regard to some of their negative effects e.g. "forever chemicals", some possess beneficial uses in medical, cosmetic, and textile industries. In this study, certain PFAS used as synthetic blood substitutes due to their high efficiency of dissolving gases were analyzed for anti-doping purposes. These compounds are banned by numerous jurisdictions in many athletic events to promote a fair and balanced environment and continued safety of athletes. The method presented here utilized headspace gas chromatography-tandem mass spectrometry (GC-MS/MS) to detect these compounds in equine serum.

This methodology consisted of a screening analysis to identify a total of 12 total PFAS in equine serum. These compounds consisted of 11 oxygen-carrying PFAS and an internal standard, bromopentafluorobenzene. The 11 PFAS with potential for use as blood substitutes were: perfluorodecalin (PFD, two isomers: *cis*-PFD, *trans*-PFD), perfluorotripropylamine(PFTPA), perfluorooctylbromide (PFOB), perfluorodecylbromide (PFDB), perfluoroadamantane (PFA), perfluoromethyladamantane (PFMA), bis(perfluorobutylethene) (F-44E), perfluoro(tert-butylcyclohexane) (PFtBCH), perfluoro[1-(4-methylcyclohexyl)piperidine] (PFMCP), 1,8-dichloroperfluorooctane (DCPFO), and perfluoromethyldecalin/perfluoro-1-methyldecalin(PFMD/PF1MD) isomers. This method was able to separate both isomers of PFD, partially separate the isomers of PFMD, and was able to differentiate between all the PFAS listed above. Limits of detection for all compounds ranged from 10-250 ng/mL using a sample volume of 100 μL of serum. The rapid analysis time of 6 minutes allowed for high-throughput analysis of equine samples for the detection of these PFAS. This methodology was utilized to examine over 70 serum samples from active racehorses.

29. QUANTIFICATION OF DEXMEDETOMIDINE IN EQUINE PLASMA AND RED BLOOD CELLS.

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Dexmedetomidine is a selective alpha-2 adrenergic receptor agonist that can be used for sedation and analgesia in multiple species. The use of dexmedetomidine in horses has become more common in recent years due to its short plasma half-life. To help institute a safe and effective anesthetic protocol, determining the pharmacokinetics and pharmacodynamics of dexmedetomidine in horses is needed. Some anesthetics have been demonstrated to partition into red blood cells, which can then serve as a depot from which the drug is slowly released. To investigate the pharmacokinetics, a quantitative LC-MS/MS method for accurately determining the concentration of dexmedetomidine in equine plasma and red blood cells (RBCs) was developed and validated. Dexmedetomidine was extracted from equine plasma and RBCs by liquid-liquid extraction with methyl *tert*-butyl ether. Medetomidine-$^{13}C,D_3$ was used as internal standard. An ACE 5 C18 column (75 x 2.1 mm) was used with mobile phases of 5 mM ammonium formate and acetonitrile. Dexmedetomidine was detected using a triple quadrupole mass spectrometer with multiple reaction monitoring in positive ion mode. The quantitative dynamic range for plasma was 10-2500 pg/mL and for RBCs was 12.5-5000 pg/g, when employing linear regression with weighing factor of $1/x^2$. The limits of detection (LOD) and quantification (LOQ) were 5 and 10 pg/mL in plasma and 5 and 12.5 pg/g in RBCs. The method was validated for extraction recovery, matrix effects, specificity, sensitivity, linearity, inter- and intra-day accuracy/precision, stability, and dilution integrity. The validated method was successfully applied to analyze plasma and RBC pilot pharmacokinetic study samples. The method is specific, accurate, and reproducibly reliable.

30. WHOLE GENOME SEQUENCING TO IDENTIFY A LARGE DELETION IN THE FBN1 GENE IN A GOLDEN RETRIEVER.

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Whole genome sequencing is underutilized as a diagnostic tool in cases of suspected genetic diseases, particularly in companion animals. Our objective was to use whole genome sequencing to diagnose a canine patient, enabling prognosis and guiding potential treatment. A client-owned, ten-month-old Golden Retriever presented with signs of possible connective tissue disorder. Blood draw, physical exam, and radiographs were performed on the patient while at the hospital, which showed clinical signs of cardiac enlargement, pneumothorax, and joint hypermobility. Whole genome sequencing was performed and genetic analysis focused on single nucleotide variants, small indels, and structural variants to detect potential disease-causing mutations within the genome. DNA samples from a non-affected German Shepherd-Beagle mix and 155 unrelated Golden Retrievers were used as controls. A roughly four-kilobase deletion encompassing exon 24 of the *FBN1* gene was detected in the patient's DNA, likely causing an in-frame deletion in the coding sequence. PCR amplification and Sanger sequencing of the suspected region was performed to confirm the presence of the deletion and the lack thereof in all controls. Previous characterizations of exon 24 being skipped in human patients also displayed clinical signs of classical MFS. The estimated impact of the deletion and the patient's associated clinical signs are highly suggestive of a dominant form of Marfan syndrome.

31. DEVELOPMENT OF NORMATIVE REFERENCE VALUES FOR GAIT KINEMATICS AND KINETICS PARAMETERS IN YUCATAN PIGS.

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Quantitative gait analysis provides an objective approach for assessing orthopedic disorders, and pigs serve as a valuable translational model due to their physiological similarities to humans. However, standardized gait parameters in pigs remain underdefined. This study aimed to establish normative spatiotemporal and kinetic gait values in healthy Yucatan minipigs using an instrumented treadmill system.

Three skeletally mature female Yucatan pigs underwent gait trials on the Zebris CanidGait treadmill following training and habituation. Walking and trotting velocities averaged 0.54 ± 0.15 m/s and 1.32 ± 0.20 m/s, respectively. Over four weeks, each pig completed 47–50 sessions, with video recordings capturing 10–15 gait cycles per trial. Parameters analyzed included stride length, cadence, stance and double stance duration, step width, symmetry index, maximum force, and peak vertical force. Outcomes were normalized to treadmill speed and assessed using mixed-effects linear regression with robust variance estimation. Marginal means with 95% confidence intervals were reported for each variable.

Results demonstrated distinct gait adaptations between walking and trotting. Trotting was characterized by longer strides, faster cadence, and reduced stance and double stance phases, while walking showed greater stability through longer stance durations and wider step widths. These findings show similarities to locomotor adaptations reported in dogs, rodents, horses, and humans, suggesting the translational potential of pig gait analysis.

Limitations include the small sample size, reliance on treadmill rather than overground locomotion, and exclusion of intermediate gaits or variable speeds. Despite these factors, this study contributes standardized reference data for pig gait parameters across two locomotor speeds.

By defining normative gait values, this work supports the use of pigs in musculoskeletal, neurological, and rehabilitation research. Instrumented treadmill analysis enables precise, reproducible evaluation of gait, strengthening the translational impact of preclinical studies on orthopedic and neurologic disorders.

32. INVESTIGATING A MYSTERIOUS NECROTIZING AND ULCERATIVE DERMATOLOGIC SYNDROME IN BULL ELK (CERVUS CANADENSIS).

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Describing the etiology, pathogenesis, and clinical effects of novel diseases in free-ranging wildlife often requires multi-institutional collaboration. These partnerships are particularly valuable when suspected cases are poorly-defined

and uncommon but affect a visible, high-profile species. We attempt to establish a case definition for a mysterious necrotizing and ulcerative dermatologic syndrome in elk (*Cervus canadensis*) and describe the investigative process, highlighting the collaboration of multiple disciplines across several universities and government agencies. From 2014 to 2020, skin biopsies or full necropsies were performed on nine elk in the Great Smoky Mountain National Park and northcentral Pennsylvania. Affected elk were adult bulls that displayed lesions throughout the year but predominantly in October through January. Bull elk had large areas of affected skin over the dorsal midline, shoulders, withers and hindquarters that ranged from patchy to regional alopecia, to crusting, ulceration and sloughed necrotic skin. Microscopically, there was epidermal and superficial dermal necrosis, granulation tissue with fibrosis, and marked secondary inflammation. Possible causes considered include photosensitization, ectoparasitism, and hereditary collagen dysplasia. Future directions and active pending tests include evaluation for possible phototoxins, perform electron microscopy on dermal collagen, and analyzing DNA for genetic mutations. Additional case solicitation is also being performed with anecdotal evidence of similar syndrome in additional states from other parts of the country. By incorporating observations of field personnel and public observers, species-specific knowledge of biologists and wildlife veterinarians, and expertise in interpreting pathologic and other changes by laboratory diagnosticians, this project utilizes each collaborator's strengths, emphasizing the importance of holistic investigations to determine the underlying cause of an undefined, uncommon, and highly visible disease.

33. ANIRIDIA IN GOS D'ATURA (CATALAN SHEEPDOG) NOT ASSOCIATED WITH PAX6.

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Aniridia is a congenital eye disorder characterized by the complete or partial absence of the iris. In humans, aniridia is associated with variants in the *PAX6* gene. It is a disease that can affect other parts of the eye, causing cataracts or optic nerve hypoplasia (ONH) among other manifestations. No known mutation has been associated with aniridia in dogs, although the association of canine *PAX6* has been previously investigated and excluded in an extended family of affected Gos d'Atura (Catalan Sheepdog) from Spain (1990s).

The lack of technology has prevented the study to continue, and the cause of aniridia in the GDA family has become a "cold case". Here we revisit the study using updated protocols, to isolate DNA from archival blood samples collected in the early 1990s. 22 Gos d'Atura dogs from two distinct pedigrees were used, with 8 of these dogs being affected. Notably, the parents of the affected dogs exhibited normal phenotypes. ONH and cataract comorbidity have been seen in only one of the aniridia-affected dogs.

Whole genome sequencing was carried out on one case, and a filtering against an internal dataset of 100+ whole-genome sequenced dogs and 2000+ publicly available dogs was carried out. We detected homozygous single nucleotide, small indels, and larger structural variants exclusive to the case, assuming an autosomal recessive inheritance, in a short list of potential candidates. Notably, a coding 34 bp deletion (of which 30 affect the exon and adjoining splice site) in the *ATP13A2* gene is being investigated as a potential candidate. WGS also confirmed the exclusion of *PAX6* and its known interactors. SNP genotyping is underway. The study highlights the potential of archival samples in the discover of novel aniridia candidate genes.

34. GALACTIC COSMIC RADIATION ALTERS DENTATE GYRUS ACTIVITY AND PATTERN SEPARATION: SEX-SPECIFIC BEHAVIORAL RESPONSES AND CDDO-EA COUNTERMEASURE EFFECTS.

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Galactic Cosmic Radiation (GCR) is an unavoidable factor in deep space travel that may affect astronaut health and mission success. Rodent studies are limited, but show that exposure to simple GCR (vs. 33-GCR) impacts cognition in a complex manner. Two measures of cognition we can assess are behavioral pattern separation (BPS), which is the ability to distinguish between similar but distinct memories and reflects integrity of the hippocampal dentate gyrus (DG), and Pavlovian learning, which reflects integrity of the nucleus accumbens (NAc). Significant knowledge gaps exist regarding cognitive effects of GCR exposure and the efficacy of anti-inflammatory interventions. We hypothesized that exposure to 33-GCR would produce sex-specific impairments in cognition, and that the synthetic triterpenoid CDDO-EA, would differentially mitigate these cognitive deficits. Here, mature C57BL/6J male and female mice received CDDO-EA or Veh for 3 days and either Sham IRR or 33-GCR (750mGy) once. Mice then underwent cognitive assessments including the Spontaneous Location Recognition (SLR) task to assess BPS, and a rodent touchscreen based autoshaping paradigm to evaluate Pavlovian learning. In the SLR paradigm, 33-GCR caused detriments in memory in male mice, and had no effect on female mice. In the autoshaping paradigm, both sexes demonstrated learning over time, but with notable sex-specific differences. When the paradigm was reversed, requiring learning adaptability, the male mice treated with CDDO-EA had improved learning, while 33-GCR had little effect. Alternatively, female mice exposed to 33-GCR had a decreased ability to learn the reversal paradigm, and those treated with CDDO-EA had decreased learning in the acquisition phase. These findings reveal sex-specific effects, where CDDO-EA enhanced cognitive flexibility in males but not females, while 33-GCR impaired learning behaviors in females but not males. Our results suggest radiation effects differ by sex, and countermeasures for deep space missions may require sex-specific approaches. This study highlights the importance of examining sex as a biological variable when evaluating potential countermeasures for space radiation.

35. GILTS TRANSITIONING FROM PEN TO CRATES EXPRESS AN INCREASE IN ABNORMAL BEHAVIORS.

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Common husbandry practices on farms today have the potential to compromise animal welfare. Confinement can inhibit the expression of species-specific behaviors and challenge natural homeostatic activities. On pig farms, an animal's social and explorative behavior is often restricted as most breeding females are confined in crates for at least

some part of their production cycle. Here, we study how the transition from group housing to the confinement of an individual stall impacts gilt behavior.

A within-subject repeated-measure study design was applied to 12 Landrace x Large White gilts that were group-housed in a collective pen for 3 weeks and then moved to individual crates for 4 weeks. Scan sampling was performed every 5 minutes between 7:30 AM and 4:30 PM on video recorded three days per week. Observed behaviors were categorized as posture (lie, stand, sit, and kneel) or activity (drink, stretch, yawn, scratch, shake head, paw surfaces, oral stereotypies, surface interaction with the snout, bite surface, social behavior, and other). Coding was performed in the BORIS software by one trained researcher with an intraobserver coefficient of variance < 5%. The data was analyzed using linear mixed models with behaviors as the dependent variable, week as a fixed effect, and day and subject as random effects to account for repeated measures. Significance level was $p < 0.05$.

Lying was the most common behavior, as animals spent 94% of their time down across the study. However, gilts in the crates laid down significantly less than animals in the pen (6.4 versus 30.2 events; $p < 0.001$). Gilts also sat more in the crates than in the pen (4.3 versus 1.4 events; $p < 0.05$). Two activities were most prevalent over the seven weeks: oral stereotypies (30.4%) and surface interaction with the snout (52.1%). These behaviors were performed more when the gilts were housed in the crates than in the pen (oral stereotypies - 15.3 versus 2.4 events; and surface interaction with the snout - 6.1 versus 1.6 events; both $p < 0.05$).

Housing impacted gilts' behavior, mainly altering their posture and activity levels. Gilts appeared busier during crate housing, both standing and sitting more, and exhibiting noted increases in select behaviors. However, oral stereotypies and excessive interaction with surfaces are not part of the species-specific swine repertoire. Individual housing increases abnormal behaviors in gilts and seems to reduce resting behavior, suggesting negative consequences for their welfare.

36. MOM IS CALLING! SOWS NURSING VOCALIZATION CHANGES WITH THE HOUSING SYSTEM.

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Conspecific communication by gregarious species like pigs is used to share important information about environmental and social conditions. We aimed to examine the effects of different farrowing systems on the nursing vocalizations of sows. One week before farrowing, pregnant gilts were weighed and allocated to either a barren (standard farrowing crate n = 11) or enriched (farrowing pens with straw, n = 13) farrowing system. Study sows shared the farrowing environment with as many as 9 other individually-housed and farrowing non-study sows. On the second or third day after farrowing, vocalizations from a single nursing bout were recorded using a microphone at 0.8 - 1m from the sow's head. The nursing bout was defined by the sow calling her piglets to nurse. The initial one-minute sample was used for call labeling based on aural and visual inspections using Raven® Pro 1.6. The total number of vocalizations labeled was 898 yielding an average of 37.5 calls per minute per sow. However, 44% of the calls had to be excluded due to overlapping contaminant acoustic signals from neighboring sows and piglets. This left 494 calls for bioacoustics analysis. The data was divided by treatment: 212 calls from barren and 282 calls from enriched farrowing systems. The data was analyzed using generalized linear mixed models with acoustic parameters as the dependent variable, treatment and body weight as fixed effects, and subject as a random effect. Significance was considered when $p < 0.05$. Results

showed no difference in body weight between the groups (Barren 219±14SDKg vs Enriched 218±16SDKg). However, the calls were longer in the sows housed in barren (0.29±0.14s) when compared to those of sows housed in enriched (0.22±0.09s) farrowing systems (p=0.045). No treatment differences were observed for low-frequency calls. However, the frequency of these calls did depend on body weight, as the dominant frequency of calls from heavier sows was lower (p=0.024). Previous work suggests that longer calls in pigs are often associated with stressful conditions and negative emotions, whereas short calls can reflect positive emotions and low stress. Our findings demonstrate that the farrow system can impact features of the nursing call and potentially influence a sow's communication with her piglets.

37. DETECTION OF CLINICALLY OVERLOOKED PATHOGENS IN WILDLIFE BRAIN TISSUE USING TARGETED-NEXT GENERATION SEQUENCING.

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Simultaneous detection of multiple infectious disease agents in diagnostic samples is critical for timely, evidence-based treatment strategies, and for limiting the spread of infectious diseases. Diseases with multiple potential etiologies, including viral, bacterial, fungal, or parasitic pathogens, usually require submission of samples to multiple laboratories, especially when clinical signs are non-specific. Targeted-Next generation sequencing (tNGS) provides a powerful tool for syndromic detection of multiple pathogens using a single assay. We tested brain specimens collected from two wildlife cases submitted to the Pennsylvania Animal Diagnostic Laboratory System- New Bolton Center (PADLS-NBC), School of Veterinary Medicine, University of Pennsylvania, for necropsy. These cases were diagnosed as encephalitis of unknown origin following testing through the molecular diagnostics, virology, toxicology, and histopathology; and after obtaining negative results for rabies, canine distemper, and avian influenza in brain and lung specimens by conventional methods. Case 1 involved a black bear (*Ursus americanus*) that died during bear trapping. Case 2 involved a fisher (*Pekannia pennanti*) that was euthanized due to abnormally aggressive behavior.

The tNGS panel, designed for the detection of multiple feline and canine infectious agents, was used to test these specimens on the Ion Torrent sequencing platform. Targeted-NGS detected *Listeria monocytogenes* in the bear brain specimen and *Leptospira interrogans* in the fisher brain specimen. These findings were confirmed by pathogen-specific real-time PCR. While detection of these agents does not establish causation, the results highlight the capability of tNGS to identify pathogens that might be missed during routine testing. This approach offers enhanced potential for diagnosing complex cases with non-specific clinical signs and could improve surveillance and our understanding of potential zoonotic threat from wildlife.

Research Grant: Mellon

38. APPLYING INFORMATION THEORY TO ANIMAL BEHAVIOR: INSIGHTS INTO LACTATING SOW BEHAVIOR AFTER RELEASE FROM TEMPORARY CRATING.

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Farrowing crates were introduced to reduce piglet mortality but confine the lactating sow, creating welfare concerns. Temporary crating offers a compromise between piglet survival and the sow's needs by allowing the sow more freedom of movement when the piglets are less susceptible to crushing. Yet questions remain about how the sudden release from confinement impacts sow behavior and their welfare. To explore this question, we have applied two measures taken from information theory, Shannon's entropy and the data compression ratio. Shannon's entropy is a measure that quantifies the information content of a symbol sequence and provides a quantitative measure of behavioral diversity. Data compression quantifies the diversity in relationships between different behaviors. We applied these novel metrics to measure diversity in behavior and diversity in the sequence of behaviors of lactating sows by video recording 36 sows from three to eight days post-farrowing. Sows were either continuously confined in closed temporary farrowing crates (n=13) or were released from crates on day four (n=12) or day seven (n=11). We found that, irrespective of treatment, after opening the farrowing crate, sows displayed greater diversity of position as well as less fixed patterning of these positions. Entropy increased from a value of 1.44 (0.97–1.93) to 2.79 (2.32–3.27), and the compression ratio decreased from 6.16 (5.08–7.13) to 3.65 (2.51–5.01) after crate opening. Farrowing crates mask individual behavioral expression as we observed noticeable individual differences in positional diversity in uncrated sows but not in crated sows. Similar results were seen when we analyzed sow activity sequences comprised of various maintenance and maternal behaviors. Taken together, these results suggest farrowing crates reduce sow welfare by limiting the free expression of species-typical behavior. Our results also highlight the applicability of entropy and data compression to behavioral analysis.

39. ADRENAL HEMORRHAGE IN AN HSV-2 EXPERIMENTALLY-INFECTED GUINEA PIG (CAVIA PORCELLUS).

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A seven-month-old female pair-housed Dunkin Hartley guinea pig was found acutely deceased. She was experimentally infected with herpes simplex virus type 2 (HSV-2) three months prior, and had no other significant clinical history of note. Vaginal swabs were performed daily by lab staff per experimental protocol. Gross necropsy demonstrated a moderately enlarged, reddened, and irregularly-shaped left adrenal gland that was diffusely hemorrhagic on cut surface. The right adrenal gland was grossly normal. Histology showed the left adrenal cortex was multifocally expanded by severe hemorrhage and necrosis. The severe multifocal to coalescing cortical hemorrhage and necrosis of the left adrenal gland with the associated historical herpesviral infection is suggestive of Waterhouse-Friderichsen syndrome. This can be induced by bacterial (*S. aureus*, anthrax, tetanus, diphtheria, *S pneumoniae*, β haemolytic streptococcus group A) or viral infection, vitamin C deficiency, or sepsis. Other differentials to consider when presented with adrenal hemorrhage in a guinea pig include adrenal hematoma, neoplasia, trauma, coagulopathies, acute stress, and autoimmune conditions.

40. BODY CONDITION SCORE, INTERLEUKIN-1β, AND INTERLEUKIN-10 PREDICT COGNITIVE CHANGES IN CLINICALLY HEALTHY SENIOR CATS.

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This study investigates the relationship between organic changes in senior cats, including low-grade chronic inflammation, and their cognition and behavior.

Data were collected from 97 cats and their caregivers: IL1β and IL10, Body Condition Score (BCS), ALT, ASP, ALP, Neutrophils, Lymphocytes, WBC, Albumin, Globulin, BUN, Creatinine, responses to a behavior questionnaire (Feline Behavior Assessment and Research Questionnaire - FeBARQ) and a cognition questionnaire (Feline Cognitive Dysfunction Syndrome Questionnaire - FCDSQ). Statistical analysis was conducted using a three-step generalized mixed model analysis to assess the association between fixed effect and confounders ($P < 0.05$).

The FCDSQ revealed that Sleep-Wake Cycle, Anxiety, Interactions, Activity, and House-soiling were significantly correlated with specific blood markers, cytokines, and BCS. Disturbances in the Sleep-Wake Cycle were directly associated with increased BCS, Globulin, ALT, ALP, Creatinine, WBC, and IL-1β, while Neutrophils and Albumin were inversely associated. Anxiety behaviors were positively associated with higher BCS, Creatinine, and IL-10, while IL-1β was inversely associated. BCS was a predictor of increased social interactions. Activity levels were positively associated with IL-10. Interestingly, BCS was directly associated with four independent variables. A one-unit rise in BCS resulted in 36% higher likelihood ($P = 0.001$) of an increase in the frequency of Sleep-Wake Cycle (disturbances), 35% higher likelihood ($P = 0.001$) in Anxiety, in a 21% higher likelihood ($P = 0.003$) of an increased frequency of (social) Interactions, and a 22% higher likelihood of increased House-soiling.

Increased body weight and changes in the inflammatory response predict cognitive changes in senior cats and should be monitored during health checks.

Research Grant: Morris Animal Foundation

41. EFFECT OF SURGICAL ANTIMICROBIAL PROPHYLAXIS DURATION FOR COLIC SURGERY ON COMPLICATIONS AND RESISTOME.

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Based on human studies, surgical antimicrobial (AMD) prophylaxis (SAP) beyond 24 hours (h) is unnecessary and potentially detrimental. The objective of this study was to compare clinical and microbiological outcomes in patients receiving 24- or 72-h of SAP for colic surgery using a prospective randomized clinical trial. Horses that recovered from colic surgery were considered. Exclusion criteria were 1) age <2 years; 2) Miniature Horses, pony and draught breeds; 3) azotemia; 4) recent hospitalization, colic surgery, or AMDs; 5) local AMD administration. Eligible horses were randomly assigned to receive SAP with potassium penicillin and gentamicin for 24- or 72-h. Clinical data and complications were compared between SAP groups. Admission and discharge fecal samples from a subset of horses (N=49) underwent

shotgun metagenomic sequencing on an Illumina platform. Reads were aligned to reference databases using the Burrows-Wheeler Aligner and taxonomic classification was performed with MetaPhlAn2.30 Sequencing reads were also aligned to the Comprehensive Antimicrobial Resistance Database (CARD)5 and characterized using the AMR++ pipeline. The microbiome/resistome was characterized and compared between SAP groups over time. One hundred and forty horses completed the study (24-h N=71 and 72-h N=69). The only clinical variable that was different between SAP groups was age. There was no significant difference between groups for any complications. Time was the main driver of changes in the microbiome/resistome: alpha diversity decreased while AMD resistance genes associated with administered AMD increased between admission and discharge. Discharge beta-lactam resistance genes were significantly higher in the 72- than the 24-h group. Based on these results, we conclude that SAP for 24-h is recommended for horses undergoing colic surgery.

Research Grant: Raymond Firestone Research Foundation

42. ELUCIDATING THE MOLECULAR ARCHITECTURE AND STRUCTURAL DYNAMICS OF PHOTORECEPTOR RIBBON SYNAPSES IN RETINAL HEALTH AND DEGENERATION VIA ULTRASTRUCTURE EXPANSION MICROSCOPY.

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Photoreceptor ribbon synapses are specialized synaptic structures that sustain high-rate transmitter release, yet their nanoscale organization and developmental dynamics in situ remain poorly defined due to the limited resolution and sensitivity of conventional immunofluorescence, especially in archival tissue of large animals. Building on our prior validation of ultrastructure expansion microscopy (U-ExM) for paraformaldehyde-fixed, cryopreserved canine retina (Takahashi K et al., *Invest Ophthalmol Vis Sci.* 2025), we used U-ExM to elucidate the molecular architecture of rod and cone ribbon synapses in retinal health and early degeneration. We applied a validated U-ExM workflow to archival canine retinal cryosections from dogs with normal retina at 2, 6, 12, and >20 weeks postnatal, and to the X-linked progressive retinal atrophy 2 (XLPRA2) model of *RPGR*-associated X-linked retinitis pigmentosa spanning early- to mid-disease stages. Confocal imaging was combined with a curated panel of >30 antibodies to map ribbon synapse-associated components together with key trans-synaptic elements. Across development in wild-type retinas, U-ExM markedly improved immunolabeling performance relative to non-expanded conditions and resolved subcompartmental organization at the nanoscale. Quantitative 3D analyses revealed progressive assembly and maturation of ribbon-associated elements. In XLPRA2 retinas, we detected early pathological changes at 6–7 weeks, including opsin mislocalization and pronounced disruption of CtBP2-labeled synaptic ribbons within degenerating zones. Together, these findings demonstrate that U-ExM provides a robust, archivable-sample–compatible framework for nanoscale mapping of photoreceptor ribbon synapses, enabling sensitive detection of early synaptic pathology in inherited retinal degeneration. Broad application of this approach across disease models should refine our understanding of ribbon-synapse architecture and dynamics, inform the timing of therapeutic interventions, and support the identification of molecular targets for preserving synaptic integrity.

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43. TESTIS SOMATIC CELL GENE REGULATORY NETWORKS UNDERLIE DRAMATIC FEEDBACK RESPONSES TO THE ABSENCE OF MALE GERM CELLS.

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Maintenance of the mammalian germ line is mediated through crosstalk between the germ cells and the somatic cell environment, but little is known about how this is regulated. Here, we employed a mouse model with one fertile and one infertile testis to compare RNA expression and chromatin accessibility at single-cell resolution between fertile and infertile states. Sertoli, peritubular myoid, mesenchymal progenitors and macrophages displayed the greatest transcriptional and epigenetic differences, with changes in genes related to growth factors, germ cell signaling, extracellular matrix and fibrosis. We generated a gene regulatory network for each cell type, identifying transcription factors (TFs), downstream regions and genes consistently altered between infertile and fertile and concentrated on factors linked via ligand-receptor pairs between somatic and germ cells. Key TFs such as *Sox9* in Sertoli cells were inferred to control downstream genes *Dhh*, *App* and *Sparc* that pair with undifferentiated spermatogonia receptors. To extend these findings to humans, we analyzed single-cell RNA sequencing data from testes of fertile and infertile patients and observed conservation in gene expression changes consistent with murine gene regulatory networks from our study. This work presents the first comprehensive network analysis of somatic cells and their response to the absence of germ cells, providing a systematic map of growth factor regulation in the mammalian testis.

44. DETECTION OF HEMANGIOSARCOMA-ODOR IN CANINE BLOOD SAMPLES BY TRAINED BIO-DETECTION DOGS.

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Hemangiosarcoma (HSA) is a common, aggressive, and deadly vascular cancer in dogs that is usually diagnosed only at advanced stages. Because treatment options are limited once HSA is advanced, earlier detection is essential to improving survival and quality of life. Five trained bio-detection dogs were evaluated using double-blinded tests using automated olfactometer line-ups. These bio-detection dogs were presented with blood serum samples from dogs with confirmed HSA, from diseased controls without HSA, and from healthy controls. All test samples were novel to the dogs. Across 423 blinded test trials, dogs achieved an overall sensitivity of 80.0%, specificity of 60.4%, and trial-level accuracy of 70% (range 58.3–78.6%). A sample-level mixed-effects logistic regression showed that dogs alerted to HSA samples in 73.4% of presentations (95% CI [68.6–77.7]), compared with 21.3% of diseased controls and 17.1% of healthy controls. Odds ratios indicated that dogs were over 10 times more likely to alert to HSA than to diseased controls (OR = 10.2, $p < .001$) and over 13 times more likely than to healthy controls (OR = 13.3, $p < .001$). This study provides the first evidence that canine olfaction can identify a unique odor signature associated with canine HSA in serum samples. These findings confirm the feasibility of volatile organic compound (VOC)–based detection of HSA and establish a foundation for future studies using chemical analysis and biosensor technology to define the compounds responsible and evaluate how early in disease progression they can be detected.

Research Grant: American Kennel Club Canine Health Foundation, with additional support from the Morris Animal Foundation, the American German Shepherd Charitable Foundation and the Rookie Fund

45. TEMPORAL DYSREGULATION OF CHONDROCYTE MATURATION AND EXTRACELLULAR MATRIX MODIFICATION FOLLOWING NEONATAL TYPE III COLLAGEN LOSS IN MURINE FEMORAL HEAD CARTILAGE.

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Osteoarthritis (OA) is a degenerative joint disease characterized by the breakdown of cartilage extracellular matrix (ECM). Cartilage repair remains elusive due to a limited understanding of ECM assembly and chondrocyte-matrix interactions. Recent evidence implicates type III collagen (COL3) as a key regulator of ECM structural integrity and cartilage health. COL3 has also been shown to regulate matrix architecture and mechanoresponses in other tissues. In this study, we hypothesize that COL3 is a critical component of cartilage ECM maintenance and repair via its roles in neo-matrix assembly and integrin-mediated mechanotransduction.

Systemic knockout of COL3 (*Col3a1* gene) was successfully achieved (mRNA levels to < 1%) following neonatal tamoxifen injection in conditional *Col3a1* knockout mice (*Col3a1*$^{F/F}$/RosaCre^{ER}, or F/F) compared to control mice (*Col3a1*$^{B6/B6}$/RosaCre^{ER}, or B6/B6). Femoral head articular cartilage was harvested either on post-natal day 21 (P21) or days 50 to 60 (P50-60) to interrogate early and later developmental timepoints. At P21, COL3-deficient cartilage exhibited an expanded hypertrophic chondrocyte zone, along with increased areal cell density and average chondrocyte area. These histomorphometric differences coincided with significant reductions in *Col2a1*, *Col10a1*, *Acan*, and *Itga10* gene expression, indicating altered dynamics of chondrocyte hypertrophy and endochondral ossification progression. *In situ* zymography revealed increased matrix metalloproteinase (MMP) activity targeting COL1 substrates, suggesting early ECM catabolic responses following COL3 loss. By P50-60, histological and transcriptional differences were largely resolved, but COL3-deficient cartilage showed a shift in ECM remodeling, with elevated MMP activity against COL4 substrates. This shift suggests a temporally distinct role for COL3 in modulating ECM modification during cartilage development.

These findings identify COL3 as a critical regulator of early chondrocyte phenotype and cartilage matrix remodeling during postnatal development and suggest a potential role for COL3 loss in accelerating cartilage degeneration and OA progression. Future studies will explore COL3's therapeutic relevance in cartilage repair and disease prevention.

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46. CLINICAL, BIOCHEMICAL, AND GENETIC FINDINGS IN AMERICAN PIT BULL TERRIER DOGS WITH MUCOPOLYSACCHARIDOSIS TYPE I.

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The mucopolysaccharidoses (MPS) are a group of inherited lysosomal storage disorders described in both humans and animals. Mucopolysaccharidosis type I (MPS I) results from pathogenic variants in the *IDUA* gene leading to a deficiency of alpha-L-iduronidase. Although several canine cases of MPS I have been reported, only a few causal variants have been identified. To date, no information on MPS I in American Pit Bull Terrier (APBT) dogs has been documented. This study describes clinical, biochemical, and genetic features of three APBT dogs affected with MPS I. Clinical information from attending veterinarians and owners revealed corneal clouding, heart murmurs, gait abnormalities, coarse metachromatic granules in leukocytes, and skeletal abnormalities, particularly affecting the cervical vertebrae. Clinical signs were observed from a juvenile age and were consistent with those previously reported in canine MPS I. Urinary metabolic analyses and alpha-L-iduronidase enzyme activity measurements revealed elevated concentrations of glycosaminoglycans, consistent with MPS, along with markedly reduced alpha-L-iduronidase enzyme activity, suggesting MPS I. To identify the underlying variant, a candidate gene approach using PCR followed by Sanger sequencing was performed. Genetic analysis identified a single-nucleotide deletion in the *IDUA* gene, leading to a frameshift and premature termination codon. The deduced amino acid sequence is truncated at residue 105, whereas the normal sequence consists of 655 residues. Further transcriptional analysis revealed that no expression of *IDUA* was detected. Based on animal variant classification guidelines, this deletion was classified as pathogenic. Notably, the corresponding variant has been reported as pathogenic in a human patient with MPS I. In conclusion, this is the first report describing the clinical, biochemical, and genetic characteristics of MPS-I in APBT dogs. These findings contribute to the understanding of genotype–phenotype correlations in canine MPS-I, and genetic testing for this variant is now available at the PennGen Laboratories.

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47. APPLICATION AND FEASIBILITY OF AUGMENTED REALITY-BASED NEURONAVIGATIONAL SYSTEM VISAR FOR INTRA-OPERATIVE BIOPSY GUIDANCE OF INTRA-AXIAL BRAIN LESIONS IN DOGS.

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Localization and accurate sampling of intra-axial lesions in the brain is challenging for neurosurgeons due to a lack of macroscopic distinction from healthy brain tissue. Intraoperative guidance, through neuronavigational systems, is thus essential for achieving adequate biopsy and resection. In veterinary neurosurgery, such systems are limited.

Here, we report the application and feasibility of using a novel augmented reality-based neuronavigational system (VisAR) for intraoperative identification and biopsy of intra-axial brain lesions in dogs. Two dogs with MRI diagnosis of intra-axial forebrain lesions suspected of gliomas underwent surgical resection using the augmented reality-based neuronavigational system (VisAR). Under routine anesthesia, a modified, bilateral, trans-frontal craniotomy was performed. Preoperative MRI data was used to create patient-specific holograms of the brain, which were projected and precisely overlayed onto the surgical field via VisAR and visualized through the surgeon's HoloLens headset. Once the location of the lesion was determined with VisAR, intraoperative ultrasound was applied at the indicated location to verify lesion presence. Further, the biopsy of the brain tissue indicated by the VisAR system was performed and collected tissue underwent histopathological evaluation. The VisAR system allowed for identification of intra-axial frontal lobe lesions in dogs. Intraoperative ultrasound confirmed the location of the lesion previously indicated by VisAR. Frontal lobe intraaxial masses in both dogs were biopsied and resected. Histopathology confirmed collected tissues were representative for pathology. Both dogs are being monitored with repeated neurological evaluations and MRI imaging. At this time, no radiological evidence of tumor regrowth has been noted. Here, we show that the VisAR system can intraoperatively guide adequate identification and biopsy of homogenous intra-axial lesions in dogs. Larger cohort studies for canine patients of different skull morphology and intracranial intra-axial lesions in various locations are needed to further validate and assess the potential, safety and accuracy of this novel technology.

48. NATURE GUIDING HOW WE NURTURE: USING THE BEHAVIORAL ECOLOGY OF THE DOMESTIC SOW TO ADVANCE WELFARE LEGISLATION.

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During the twentieth century, pork production transitioned from small extensive farms to large intensive systems, leading to widespread confinement of commercial sows. This global intensification of pig production generated substantial welfare concerns, including questions about the expression of maternal behaviors. Ethologists often use the behavioral repertoire of wild animals to understand the ecological and welfare needs of their domestic counterparts. Thus, we hypothesized that the welfare of today's commercial sow will depend, at least in part, on 1.) evidence that the domestic sow maintains the motivation to perform those behaviors intrinsic to the wild sow, and 2.) evidence that suppression of these behaviors results in measurable indicators of negative welfare. We compiled evidence from the literature to investigate the maternal behavioral repertoire of the wild sow during each stage of her reproductive cycle and the domestic sow's enduring motivation to perform these behaviors. Our findings detail the survival of the wild sow's maternal behavioral repertoire within the modern-day domesticate and the negative welfare outcomes associated with inhibition of these behaviors under most commercial conditions. Using this ethological framework, we examined California's Proposition 12 to identify opportunities to advance welfare through housing legislation informed by a sow's behavioral ecology. Collectively, this work substantiates the use of wild sow behavior as a comparative framework to assess the welfare outcomes of commercial sow housing and highlights the critical role that animal behavior science should play in shaping evidence-based policy.

NOTES

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