December 2024

UC DAVIS
VETERINARY MEDICINE
Center for Equine Health

2024 CENTER FOR EQUINE HEALTH

RESEARCH REVIEW

New Discoveries in Equine Health

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December 2024

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The Center for Equine Health is partially supported with funds provided by the State of California Pari-Mutuel Fund and contributions by private donors.

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On the cover:

Front cover - Deborah Butterfield, Bow Tie, 2021-2022, cast bronze with patina, 85 x 105 x 36 inches. Photo Credit: Walla Walla Foundry.

Back cover - Deborah Butterfield, Portal, 2022-2023, cast bronze with patina, 91 x 86 x 43 inches. Photo Credit: Walla Walla Foundry.

Director's Message – Research Review

We are proud to present the 2024 Research Review, focused on the research accomplishments of UC Davis faculty, residents, students, and staff as supported by the Center for Equine Health (CEH).

Regardless of whether the conversation focuses on racehorses, show horses, or pleasure horses, research to improve equine health and welfare is more important than ever to the continued success of the equine industry. The Center's mission is to support equine teaching, research and service activities essential to the UC Davis School of Veterinary Medicine. UC Davis researchers investigate the genetic basis for a variety of conditions, seek ways to improve detection and management of infectious diseases, employ cutting-edge imaging and surgical approaches for orthopedic injuries, advance equine reproductive technologies, and much more.

This review also highlights research performed by UC Davis veterinary residents. Research opportunities for resident and graduate students are essential for training the next generation of equine clinician scientists. The CEH grant program provides residents with firsthand experiences, from writing grants to generating results, analyzing data, and publishing their findings.

We would like to extend a special thanks to artist and UC Davis alumna Deborah Butterfield for sharing images of her sculptures for our cover. We had the pleasure of hosting Debby for a visit at CEH during the installation of her exhibit *P.S. These are not horses* at the Jan Shrem and Maria Manetti Shrem Museum of Art here at UC Davis. Her love of horses was apparent, and our Teaching Herd horses took to her immediately. We truly enjoyed spending time with this amazing artist and fellow equestrian.

The research presented here is made possible by the generosity of our donors who continue to invest in CEH for the health and happiness of horses in California and beyond. ***Thank you*** for your support!

Carrie J. Finno, DVM, Ph.D., DACVIM
Director, Center for Equine Health

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CENTER FOR EQUINE HEALTH AWARDS

2022 James M. Wilson Award – Erin Hales, PhD


Dr. Erin Hales

Dr. Hales was chosen for her publication entitled, "Postmortem diagnoses of spinal ataxia in 316 horses in California," published in the Journal of the American Veterinary Medical Association.

Hales completed her PhD in animal biology at UC Davis under the mentorship of Dr. Carrie Finno. Her work focused on equine neuroaxonal dystrophy/equine degenerative myeloencephalopathy (eNAD/EDM), an inherited neurodegenerative disorder linked to a vitamin E deficiency. Her research identified cervical vertebral compressive myelopathy (CVCM or wobblers), equine neuroaxonal dystrophy/equine degenerative myeloencephalopathy (eNAD/EDM), and trauma as the leading causes of diagnosable ataxia. This research has helped give veterinarians some insight into which disease may be affecting an ataxic horse in their care.

Dr. Hales currently uses her knowledge of biological processes and statistics to evaluate and improve personalized medicine in her current role at SomaLogic. She continues to be active in her local equine community and is always looking for ways to bring equine medicine and research together.

James M. Wilson Award

The James M. Wilson Award highlights an outstanding equine research publication authored by a graduate student or resident in the UC Davis School of Veterinary Medicine. Center for Equine Health Scientific Advisory Board members judge the papers based on scientific merit, quality of writing and relevance to the equine industry. Dr. Wilson was a 1945 graduate of the Ohio State University College of Veterinary Medicine. He was a well-known and respected racetrack veterinarian in California and maintained a strong interest in equine research at UC Davis.

2022 and 2023 James M. Wilson Award – Sarah Shaffer, PhD

Dr. Shaffer completed her PhD in Mechanical and Aerospace Engineering at UC Davis at the J.D. Wheat Veterinary Orthopedics Research Laboratory (VORL) under the supervision of Drs. Susan Stover and David Fyhrie. Her research focused on how proximal sesamoid bone (PSB) fractures develop in racehorses. The PSBs are a pair of bones in the forelimb of horses and PSB fracture accounts for nearly 50% of racehorse deaths in the United States.


Dr. Shaffer and her horse Beau

In 2022, Shaffer was honored for her publication, "In vitro motions of the medial and lateral proximal sesamoid bones under mid-stance load conditions are consistent with racehorse fracture configuration," published in the Journal of Biomechanics.

Shaffer's publication "Training drives turnover rates in racehorse proximal sesamoid bones", in the journal Scientific Reports, was selected in 2023.

Shaffer's research helps explain the relationship between PSB fracture, internal biological changes in PSB morphology in response to mechanical loading, and racehorse training and racing history. She recently began a new role as a Research Engineer at the Southwest Research Institute.

2022 Louis R. Rowan Fellowship – Christina Rohlf, PhD

A doctoral graduate in biomedical engineering, Rohlf conducted her research at the J.D. Wheat Veterinary Orthopedics Research Laboratory under the direction of Dr. Susan Stover.

Rohlf's research focused on optimizing the interface between equine locomotion and performance surfaces, with the goal of preventing the most common injuries to tendons and ligaments associated with repetitive motions incurred during training and competition. She also obtained limb kinematic data from horses jumping on the same surfaces to determine the effect of surface shear and vertical impact surface properties on limb motion. Using these

data, she is determining the flexor tendon and suspensory ligament strains associated with different surface properties, which are likely related to risk for injury.


Dr. Christina Rohlf

Developing a set of standards for arena surface properties designed to minimize tendon and ligament injuries will guide construction and management of arena surfaces that reduce injury risk for horses in training and competition.

In her spare time, Rohlf volunteers as a mentor for the Woodland High School robotics team where she teaches engineering design principles and teamwork. She hopes to continue conducting research to understand and reduce the risk of musculoskeletal injuries in animal athletes.

Louis R. Rowan Fellowship

The Louis R. Rowan Fellowship, funded by the California Thoroughbred Foundation with financial assistance from the Oak Tree Racing Association, was established in memory of one of the California Thoroughbred Foundation's founders. In addition to being a noted racehorse owner and breeder, Rowan was active in many areas that benefitted people and horses in the Thoroughbred world.

2023 Louis R. Rowan Fellowship – Shadira Gordon

Shadira Gordon is a DVM, MPVM, and PhD student in the Graduate Group in Epidemiology. She conducted a case-control study to evaluate the effect of host characteristics, diet, and biosecurity protocols in performance horses in California during a multicounty equine herpesvirus 1 (EHV-1) outbreak. Her results pinpointed crucial factors influencing EHV-1 susceptibility, such as how often horses attend competitions, the number of horses attending from the same facility, and the nature of competitive activities, which provide evidence for the critical role of stress and latency in EHV-1 development among performance horses.

Gordon is also working to identify and categorize genetic variants in EHV-1 strains isolated during the California EHV-1 outbreak. The goal is to integrate potential prevention strategies, the genetic characteristics of the virus, and analyses of horse movements between events. This will provide an improved understanding of the transmission dynamics and future directions for effective disease control.

Beyond her research, Shadira is a strong advocate for One Health initiatives. She envisions her research making a practical impact by fostering collaboration among horse trainers, stakeholders, and veterinarians. Her work aims to develop effective strategies for performance horses, potentially serving as a model for addressing other equine infectious diseases locally and internationally.

RESOURCE FUNDS

Center for Equine Health Directorship Support Fund – This fund was established by the estate of Joyce E. Williams in 2015 to provide support funds to the CEH director.

Director's Endowment – The Director's Endowment provides general funding for Center for Equine Health research, educational or welfare activities most critical to the needs of the horse in any given year. This endowment also provides the foundation for all Center endeavors.

Gregory L. Ferraro Endowed Directorship – This endowment was established in 2015 in honor of Dr. Gregory L. Ferraro, director emeritus of the Center for Equine Health, for his lifelong dedication to advancing the health and welfare of horses. The fund provides support to the director to develop the vision and plan for the enduring success of the Center.

Polly and Bill Swinerton Director's Endowment – This fund supports the activities of the Center for Equine Health Director to advance the facility's teaching, research and service missions.

William and Inez Mable Family Foundation Endowment – This endowed fund was established to support the Center for Equine Health in its operational, educational and research efforts. Endowment earnings are distributed at the direction of the Center Director for advancing the health, well-being, performance, and veterinary care of horses through research and/or education.

INNOVATION FUNDS

Alamo Pintado Equine Health Foundation Fund – This fund was established in memory of Doug Herthel to support equine biomarkers of neurologic disease research at the Center for Equine Health.

Animal Rescue and Disaster Medicine Endowment – The Animal Rescue and Disaster Medicine Endowment supports the development of improved techniques for the rescue of large animals during natural disasters. The fund also provides for research into medical conditions of the animals and the development of improved treatment regimens.

Bernard and Gloria Sallck Equine Viral Disease Laboratory Endowment – This endowment supports a program dedicated to international scientific investigations of emerging equine viral diseases. Its goal is to identify and control viral diseases of the horse that can affect the international movement, commerce and health of competitive equine athletes.

Center for Equine Health General Research Fund – A research fund established to allow gifts of any size to be aggregated and used for research priorities at the Center for Equine Health.

Center for Equine Health Teaching Herd Endowment – Fund established to create long-term support for the care of the horses housed for teaching purposes at the Center for Equine Health.

Dan Evans Memorial Endowment – The Dan Evans Memorial Endowment provides funding for UC Davis veterinary hospital resident house officers to conduct research in any area of equine medicine and surgery that is relevant to the development of their specialty board certification.

Enduring Legacy Endowment – The Enduring Legacy Endowment was established to provide for the administration of high-risk therapies to severely ill or injured horses with unique veterinary conditions for which there is a high degree of learning value associated with their condition. The fund also supports clinical trials within the School of Veterinary Medicine.

Equine Athletic Performance Laboratory Endowment – The Equine Athletic Performance Laboratory Endowment provides for the development of analytical methods for accurately evaluating the athletic conditioning and performance capability of individual horses. Once these analytical techniques are fully developed, the goal of the program is to provide an objective evaluation of the ability of drug agents and training methods to enhance performance and decrease the risk of injury in competitive horses.

Equine Herpes Virus Research Fund – Established by gifts from the Desert International Horse Park and the US Hunter Jumper Association for purposes of supporting research into equine herpes virus 1 (EHV1) and the associated neurologic disease equine herpes myeloencephalopathy (EHM) at the Center for Equine Health.

Equine Infectious Disease Fund – Established by a 2022 gift from the Harriet E. Pfledger foundation for the purpose of supporting equine infectious disease research.

Equine Tribute and Memorial Fund – The Equine Tribute and Memorial Program provides an opportunity to pay tribute to or memorialize special horses. Gifts to the fund provide support to research studies sponsored by the Center for Equine Health.

Eve Lloyd Thompson Endowment – Fund established in 2021 by the estate of Eve Lloyd Thompson to support medical research for the benefit of horses.

James M. Wilson Endowment – Established in 1995 to honor Dr. James M. Wilson, the fund supports an annual award recognizing an outstanding resident or graduate student researcher.

J.D. Wheat Veterinary Orthopedic Research Laboratory Endowment – The J.D. Wheat Veterinary Orthopedic Research Laboratory investigates the underlying causes of bone fractures, their prevention, and new methods of fracture repair. This Laboratory was originally established by the Southern California Equine Foundation, Inc., with funds provided by the Dolly Green Research Foundation.

John P. Hughes Memorial Endowment – Named after the founding director of the Center for Equine Health, the John P. Hughes Memorial Endowment provides funding for UC Davis veterinary hospital resident house officers to conduct clinical research in any area of equine medicine or surgery.

Juliette Weston Suhr Fellowship Fund – The Juliette Weston Suhr Fellowship is awarded to postgraduate veterinary students who are interested in conducting research in the areas of exercise-related cardiopulmonary and metabolic disorders.

Lorna Talbot Equine Biomedical Fund – Established by Lorna Talbot in 2003, the fund promotes the development of new and re-emerging research programs in basic equine sciences.

Lorna Talbot Equine Clinical Program – Established by Lorna Talbot in 2003, the fund promotes the development of new medical programs of clinical relevance with the UC Davis veterinary hospital.

Lucy G. Whittier Endowment for Equine Perinatal and Infectious Disease – The Lucy G. Whittier Endowment is dedicated to improving the health and medical treatment of newborn foals and their dams, and to conduct research on infectious diseases associated with foals.

Patricia J Hobbs Endowed Research – Established by the estate of Patricia J Hobbs in 2009 to support research in the field of equine laminitis.

Patricia Yeretzian Endowment Fund – Established by longtime Silver Stirrup Society members, Patricia and Paul Yeretzian, this fund supports equine research projects relating to reproduction and infertility disorders.

Peray Memorial Endowment – The Peray Memorial Endowment is an important resource for resident house officers of the UC Davis veterinary hospital to conduct equine respiratory disease and colic research.

Performance Horse Endowment – This endowment focuses on medical problems of the mature show and event horse and funds long-term, in-depth studies of problems that preclude horses from performing athletically as they age. Areas of study include colic, nutrition, cardiopulmonary health, degenerative orthopedic processes, and infectious disease.

Platinum Performance Nutrigenomic Research Fund – This fund was established in 2019 by Platinum Performance to perform precision medicine in horses by expanding the phenotypic dataset currently collected on individual horses in the Center's teaching herd to include genotype data.

Robert C. Caldwell Fund – Established in 2011, this gift supports research related to metabolic diseases that are causative of, or related to, laminitis in horses.

Sundance Ranch Endowment – This fund was established by the late Carol Green to provide funding support for research in biological and translational research in the pursuit of effective treatments and cures for systemic diseases of the horse. Ms. Green had particular interest in medical conditions related to the development of laminitis.

Simulcast Racing Contributions

In 1987, the Satellite Wagering Act (Senate Bill 14) designated one-tenth of one percent of California's simulcast racing handle to be used for equine research. In 1994, Senate Bill 518 was passed, designating the redistribution of the simulcast racing percentage. These funds support both the Center for Equine Health and the Kenneth L. Maddy Equine Analytical Chemistry Laboratory. This important laboratory has three components: (1) a full-service, routine drug testing program, (2) a forensic toxicology program, and (3) a pharmacology research and methods development program. The latter includes the development of new tests and documentation of drug testing effects on racehorse performance. In 2001, the Account Wagering Bill (Assembly Bill 471) was passed, directing simulcast contributions made through televised wagering to UC Davis equine research and drug testing programs.

COMPLETED RESEARCH STUDIES

DRUG THERAPIES

Morphine concentrations in horses following oral administration: a new investigation of an old drug

(Grant #21-E)

Investigators: Heather Knych, DVM, PhD, DACVCP

Morphine is an effective pain reliever used commonly in human and small animal medicine. In some species, pain control effects of morphine have been attributed, at least in part, to one of the metabolites called M6G. In a crossover design, eight horses were given a single intravenous (IV) dose of 0.2 mg/kg morphine or oral doses of 0.2, 0.6, and 0.8 mg/kg of morphine. Levels of morphine and metabolites were determined. Physiologic and behavioral outcomes, including the number of steps taken, changes in heart rate, and gastrointestinal sounds were assessed. Oral administration of morphine resulted in higher concentrations of morphine metabolites, including M6G (maximum concentration: 11.6-37.8 ng/mL (0.6 mg/kg); 15.8-42.6 ng/mL (0.8 mg/kg)), as compared to IV. Oral absorption was moderately low (bioavailability was 36.5%, 27.6% and 28.0% for 0.2, 0.6 and 0.8 mg/kg, respectively). Behavioral and physiologic changes were noted in all groups but were less pronounced with oral administration compared to IV administration. These results are encouraging for further study, specifically of pain relieving effects of morphine following oral administration.

How does this research benefit horses? The study sought to investigate the behavior of a potent pain reliever when administered orally to horses as an important first step in assessing the utility of this method of administration for pain control, with the ultimate goal of adding to currently limited options for pain relief in horses.

This research was reported in *J Vet Pharmacol Therap* 2023; 46(4), 238-249.

GENETICS

Confirming a genetic mutation for inherited hypocalcemia in Thoroughbred foals

(Grant #19-16)

Investigators: Carrie J. Finno, DVM, DACVIM (LAIM), PhD; Gary Magdesian, DVM, DACVIM (LAIM), DACVECC, DACVCP; Mustafa Khoka, PhD; Andrew D. Miller, DVM, DAVP

A syndrome of low blood calcium concentrations, leading to stiffness, weakness, and death, has been described in Thoroughbreds foals since 1997. With support through the Center for Equine Health in 2017, we identified a possible genetic mutation for this inherited disease. This grant confirmed the genetic mutation for this disease by testing two additional Thoroughbred foals and providing functional support for the genetic mutation in the gene *RAPGEF5*. This led to a DNA test that is now available through the UC Davis Veterinary Genetics Laboratory.

How does this research benefit horses? Confirming the genetic mutation for inherited hypocalcemia of Thoroughbred foals has allowed DNA testing to screen for potential carriers and avoid breeding of carriers to carriers. Additionally, the implication of *RAPGEF5* in a disease that leads to widespread hypocalcemia in the horse has strong implications across species.

This research was reported in *PLOS Genetics* 2020; 16(9):e1009028. The genetic test is available at UC Davis: https://vgl.ucdavis.edu/test/efih.

To obtain additional information on a research study, please reference the grant number in your request.

Validating a biomarker test for equine neuroaxonal dystrophy/degenerative myeloencephalopathy

(Grant #19-17)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM)

Equine neuroaxonal dystrophy/degenerative myeloencephalopathy (eNAD/EDM) is one of the top three causes of spinal ataxia in horses and is characterized by incoordination that typically develops in young foals 6-12 months of age. Currently, there is no diagnostic test available for eNAD/EDM other than an examination following euthanasia. In 2017, a Center for Equine Health funded resident project by Dr. Lisa Edwards supported the pilot investigation evaluating a biomarker of axon damage called phosphorylated neurofilament heavy subunit (pNfH) in horses with eNAD/EDM. We expanded upon this pilot study by sampling additional eNAD/EDM affected and unaffected horses in this current grant. We found that blood pNfH concentrations >1 ng/mL were significantly associated with eNAD/EDM (P =0.01), with only 12% sensitivity but 99% specificity. Spinal fluid pNfH concentrations >3 ng/mL were significantly associated with cervical vertebral compressive myelopathy (i..e "Wobbler's disease; P = 0.0002), with 50% sensitivity and 86% specificity. This test became commercially available through the UC Davis Clinical Pathology Laboratory.

How does this research benefit horses? A supportive diagnostic test for eNAD/EDM has provided veterinarians the necessary information to make informed decisions about horses with neurologic disease. As there is currently no effective therapy for eNAD/EDM, if this disease is diagnosed, an owner can make an informed decision to either euthanize or maintain the horse as a non-riding and non-breeding horse.

This research was reported in *Equine Vet J* 2022; 54(2):290-298.

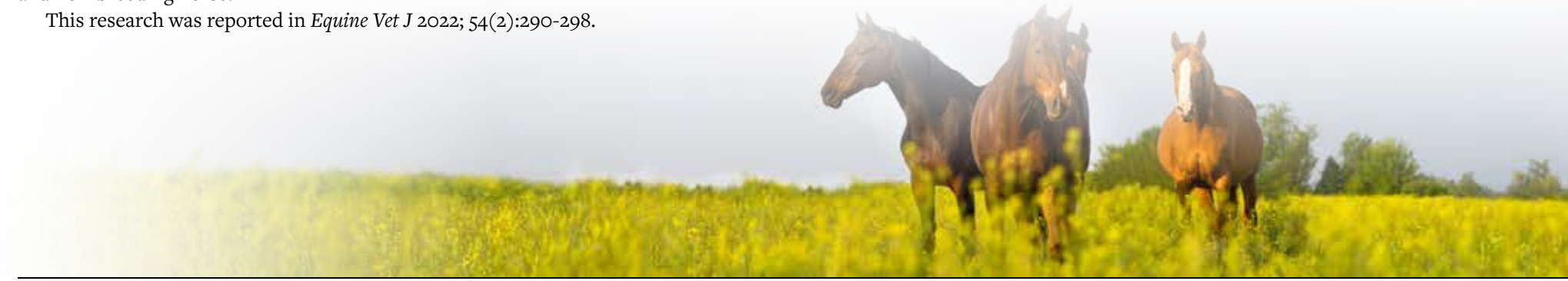
Validating a genetic test for a bleeding disorder in Thoroughbred horses (Grant #19-18)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM), Fern Tablin, VMD, PhD

Atypical equine thrombasthenia (AET) is a clotting disease that appears to be inherited in the Thoroughbred (TB) breed. Horses with AET have abnormal bleeding after injury. AET may also lead to bleeding from the airway, which is also the hallmark sign of exercise-induced pulmonary hemorrhage (EIPH). However, EIPH is only associated with bleeding from the airway post-exercise and affected horses do not demonstrate other problems with clotting. There is currently no way to distinguish between AET and EIPH in TBs without extensive specialized laboratory testing. Therefore, there is no way to predict if a nosebleed is due to EIPH or to the more serious clotting abnormalities of AET. The development of a genetic test for AET would allow for rapid diagnosis and breeding management. In this study, we defined the effects of a previously identified strong candidate missense mutation in suppressor/enhancer of lin-12-like (SEL1L) for AET. We confirmed that this is the most likely genetic candidate for this disease in Thoroughbred horses.

How does this research benefit horses? On one breeding farm, AET was estimated to affect one in every 150 Thoroughbreds, causing bleeding from the airway with exercise and prolonged bleeding after injury. AET may also negatively affect a horse's racing career due to repeated bleeding episodes. With the high prevalence of this disorder, a genetic test is required for accurate and prompt diagnosis. This genetic test is now part of a bleeding panel genetic screen that is available at UC Davis Veterinary Genetics Laboratory.

This research was reported in *Equine Vet J* 2021;53(1):30-37.



Validating a genetic susceptibility to melanoma in graying Connemara ponies (Grant #19-19)

Investigators: Carrie J. Finno, DVM, PhD, DAVIM (LAIM), Alain Théon, DVM, PhD, DACVR-RO


Gray pony

Melanoma in graying horses is a hereditary disease with a complex mode of inheritance. Other than the graying mutation itself, no additional genetic associations have been identified for the risk of melanoma in graying horses. With support from the Center for Equine Health in 2017, we sequenced the entire genome of eight early onset (i.e. by 6 years of age) graying Connemara ponies with melanoma; six late onset (i.e. > 15 years of age) graying Connemara ponies with melanoma; and four graying Connemara ponies with no melanoma identified by 15 years of age. When comparing the early onset cases to either the unaffected cohort alone or the unaffected cohort plus the late onset cohort, a large region on chromosome 1 within a known tumor-suppressor gene (CAPN9) was identified. Because mutations of tumor-suppressor encoding-genes are common genetic abnormalities associated with inherited cancers, we hypothesized that this genetic region in CAP9N is associated with increased melanoma risk within graying Connemara ponies. In this study, we were unable to validate the association of the CAPN9 genetic region to melanoma susceptibility in graying Connemara ponies. Therefore, this genetic region does not appear to be associated with melanoma in graying Connemara ponies.

How does this research benefit horses? Horses with graying hair coat have an 80% risk of developing melanoma. Graying ponies may develop melanoma late in life that is usually associated with a slow evolution and less likely to be life threatening. However, graying ponies that develop melanoma early in life are at high risk of dying of the disease because of faster evolution and earlier metastatic spread and represent a significant commercial loss for the industry. A susceptibility test for equine melanoma in graying horses would enable veterinarians to identify graying horses at high risk of early onset disease and monitor these individuals closely for tumor development.

Identifying a genetic mutation for a new neurologic disease in Quarter Horse foals (Grant #20-1)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM), Kevin D. Woolard, DVM, PhD, DACVP

In 2020, we identified six related Quarter horse foals that developed a severe neurologic disease between 1 and 4 weeks of age. These foals became uncoordinated and demonstrated severe weakness of their hindlimbs, culminating in the inability to stand within 3 to 7 days. Due to the poor prognosis, the foals were euthanized. Investigation after death identified lesions within the spinal cord. Based on pedigree analysis, the disease appeared to be inherited as an autosomal recessive trait. We performed whole-genome sequencing of four affected foals and their parents to identify the causative genetic variant. This study led to the identification of a genetic region on chromosome 11 that contained the genetic cause for this disease.


A Quarter Horse foal affected with a newly identified neurologic disease.

How does this research benefit horses? Identifying a genetic mutation for this new neurologic disease in Quarter horse foals allows for DNA testing to screen for potential carriers and avoid breeding carriers to other carriers.

This research was reported in *J Vet Intern Med* 2024;38(3):1808-1814.

Investigation of a candidate gene for equine neuroaxonal dystrophy (Grant #20-2)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM)

Equine neuroaxonal dystrophy (eNAD) is an inherited neurologic disease in horses. Both a genetic susceptibility and a vitamin E deficiency during the first year of life are required for a foal to develop eNAD. Through previously funded studies from the Center for Equine Health, we localized the genomic region of interest to chromosome 7 (chr7), which contained 147 candidate genes. We subsequently refined the region to 46 prioritized genes and excluded one of these, *ATCAY*. Based on exciting new data evaluating the non-antioxidant role of vitamin E, one of the 46 remaining genes, *acyl-coA synthetase bubblegum family member 2* (*ACSBG2*), was a very strong candidate. In this study, we tested an additional cohort of eNAD-affected and unaffected horses for variants in this gene. The possible association of this genetic region with eNAD was excluded in this larger population of horses. We also completed a retrospective study showing that eNAD was the second most common cause of spinal ataxia in horses seen at UC Davis. Additionally, we demonstrated that horses with eNAD metabolize vitamin E faster than unaffected horses.

How does this research benefit horses? While we have demonstrated success in identifying a biomarker (pNfH) for eNAD, overall sensitivity is quite low. Therefore, a genetic test is still required to definitively identify eNAD-affected horses. Susceptible foals could be supplemented with a high dose of vitamin E at birth to prevent disease development.

This research was reported in *J Am Vet Med Assoc* 2021;258(12):1386-1393; *J Vet Intern Med* 2021;35(5):2473-2485; *J Vet Diagn Invest* 2021;33(3):506-515; *Drug Test Anal* 2021;13(6):1158-1168.

Confirming genetic markers for juvenile idiopathic epilepsy in Arabian horses (Grant #20-6)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM); Monica Aleman, MVZ, PhD, DACVIM (LAIM and Neurology), Tatiana Vinardell, DVM, PhD

Juvenile idiopathic epilepsy (JIE) is a disorder of Egyptian Arabian foals that causes seizures and has potential life-threatening complications, including head injury and aspiration pneumonia. Currently, there is no genetic test available for JIE. Through support from previous grants funded by the Center for Equine Health, we successfully mapped the genetic location for the JIE mutation to chromosome 1. As new cases of JIE are exceedingly rare at UC Davis, we have been unable to validate these genetic markers in another set of cases and controls. However, we developed an exciting collaboration with Dr. Tatiana Vinardell at the Equine Veterinary Medical Center in Qatar to obtain samples from additional JIE-affected cases and controls. With these samples, we were able to exclude that the candidate region on chromosome 1 is associated with JIE.

An Egyptian Arabian horse.

How does this research benefit horses? Epilepsy can result in loss of animals and is a major financial burden due to costs of antiepileptic treatment. Identification of genetic variants will aid in strategic breeding to improve the overall health of the Arabian breed. Additionally, our findings may have strong implications for human health.

Investigating the genetic connection between coat color and eye diseases in the horse (Grant #20-18)

Investigators: Rebecca Bellone, PhD, Callum Donnelly, BVetBiol/BVetSc, DACT, DACVIM, Kelly Knickelbein, VMD, DACVO, Felipe Avila, PhD, Sara Thomasy, DVM, PhD, DACVO

Horses have been selected for coat color since their domestication. The variety of colors and patterns is of great interest to the industry, but genetic components have only been identified for some of the variations. We extensively characterized coat color, white patterning, and countershading in a cohort of 99 horses from 17 different breeds at two time points (winter and spring). Additionally, we performed chemical analysis on fifteen horses to determine specific melanin pigment type and ratio in different areas of the body. Combined with the Pioneer 100 Horse Health Project whole genome sequencing data, an association analysis was performed that allowed us to rule out candidate causal variants for some of the coat color phenotypes observed in this cohort. These data together provide the basis for future studies to expand our knowledge of pigmentation biology in the horse.

Dr. Callum Donnelly (left) preparing a horse for an ocular examination.

Previous research has documented a link between some coat colors and ocular disorders. Therefore, we also evaluated the eyes of 41 horses by performing complete ocular exams and dark and light adapted electroretinography (ERGs). We genotyped these horses for the genetic variant (CSNB2), found previously to cause night blindness (inability to see in dark conditions) in one Tennessee Walking Horse. While there was no link between CSNB2 and coat color, these data confirmed CSNB2 as causal for night blindness across three different breeds (Tennessee Walking Horse, Standardbred, and Missouri Fox Trotter) and identified CSNB2 in six other breeds, suggesting night blindness is underdiagnosed in the horse.

How does this research benefit horses? This work expanded the knowledge of the genetics of night blindness in the horse, with CSNB2 only the second reported variant to be confirmed to cause night blindness. This work supports the use of genetic testing for CSNB2 to avoid producing animals that cannot see at night, particularly in those breeds noted to have the variant.

This research was reported in *Vet Ophthalmol* 2024;27(3):248-255.

The genetics of equine neuroaxonal (eNAD) dystrophy in Gypsy Vanner Horses (Grant #22-B)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM)

Equine neuroaxonal dystrophy (eNAD) is an inherited neurologic disease in horses. Both a genetic susceptibility and a vitamin E deficiency during the first year of life are required for a foal to develop eNAD. Our previous work, funded through the Center for Equine Health, has extensively studied this disease in Quarter Horses (QHs). In eNAD-affected QHs, we have demonstrated increased vitamin E metabolism, identified the phosphorylated neurofilament heavy chain (pNfH) biomarker that, when elevated in serum, is highly specific (but not sensitive) for eNAD, and identified candidate genomic regions of interest. Despite years of effort, we have been unable to develop a genetic test for eNAD in the QH. However, we have recently identified a cohort of Gypsy Vanner Horses in the United States with confirmed eNAD. With only 2,200 Gypsy Vanner horses currently residing in the US, this limited gene pool may provide the necessary samples to uncover the genetic cause for eNAD. In this study, we clinically defined eNAD in the Gypsy Vanner horse and determined genomic regions of interest that overlapped with those in the QH.

A Gypsy Vanner Horse showing neurologic defects related to eNAD.

How does this research benefit horses? While we have demonstrated success in identifying a biomarker (pNfH) for eNAD in the QH, overall sensitivity is quite low. Therefore, alternate biomarkers or a genetic test is still required to definitively identify eNAD-affected horses. Susceptible foals could be supplemented with a high dose of vitamin E at birth to prevent disease development.

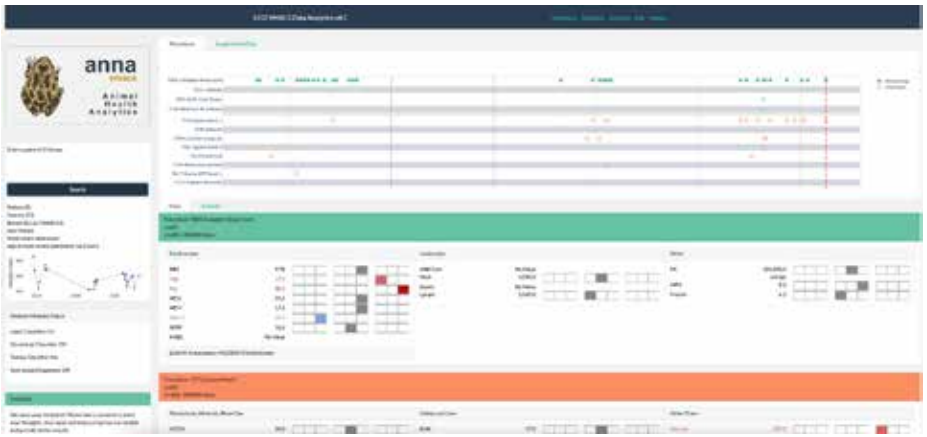
This research was reported in *J Vet Intern Med* 2024;38(3):1792-1798.

MATHEMATICAL MODELS

Integrating artificial intelligence into equine diagnostics (Grant #21-Y)

Investigators: Stefan Keller, DVM, Dr Med Vet, PhD, Krystle Reagan, DVM, PhD, DACVIM (SAIM), Titus Brown, PhD, Chris Brandt, DVM, MS, Allison Zwingenberger, DVM, MS, DACVR, DECVRI

Artificial intelligence (AI) has the potential to positively impact patient care; however, the UC Davis veterinary hospital has been lacking the computational infrastructure to apply AI algorithms to patient data in real time. This project created ANNA, an animal health analytics platform that can visualize laboratory data and apply AI algorithms to patient data. The development of ANNA was supported by joint funding from the Center for Equine Health and the Center for Companion Animal Health, and its vision is to provide data analytics services for multiple species. ANNA is a cloud-based application that can be accessed through a patient's electronic medical record or directly via URL from anywhere with an internet connection. ANNA provides an intuitive overview of laboratory procedures performed on a patient including automated grading of abnormalities of routine blood parameters and data trends over time. We have demonstrated ANNA's functionality to provide AI analyses in real-time by implementing AI classifiers for the detection of Addison's disease and Leptospirosis in dogs. In addition to viewing AI analysis results by visiting the ANNA website, ANNA can display classifier results directly in the electronic medical records system. Our lab is working on an AI classifier to interpret routine blood work, which will be deployed on ANNA when ready.



ANNA software

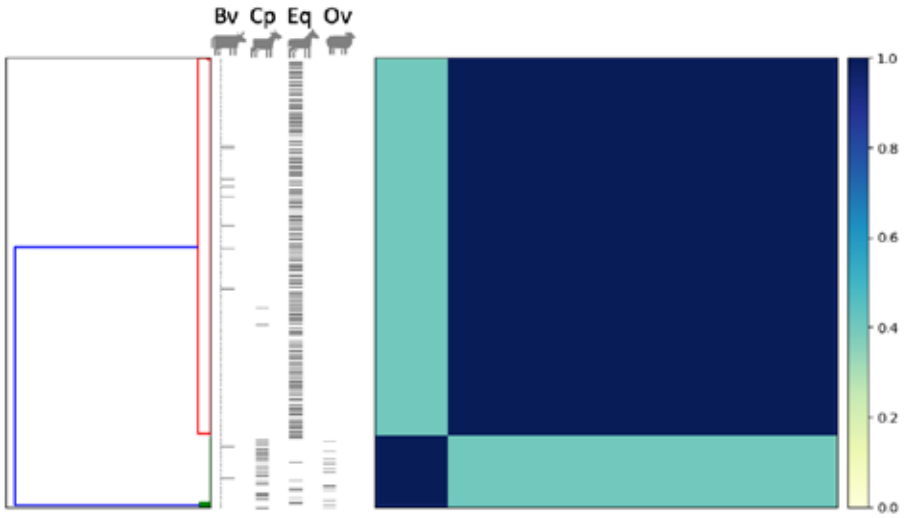
How does this research benefit horses? Creating the computational infrastructure to facilitate the interpretation of test results by artificial intelligence will further elevate the level of medical care delivered to equine patients at UC Davis and will provide critical training for the concept of AI support for clinical decision making to the next generation of veterinarians.

MEDICINE & INFECTIOUS DISEASE

Investigating Effective Antibiotic Treatments for Equine *Corynebacterium pseudotuberculosis* Infections Using Longitudinal Comparative Population Genomics (Grant #20-5)

Investigators: Bart Weimer, PhD, Vasco Ariston De Carvalho Azevedo, DVM, PhD, Barbara A. Byrne, DVM, PhD, DACVIM (LAIM), DACVMBM, Cory L. Schlesener, Bihua C. Huang, Ashleigh Flores, MS, Rodrigo Profeta

The pathogenic bacteria species *Corynebacterium pseudotuberculosis* (*C. ptb.*) is an understudied organism that persistently infects horses and livestock. We performed whole genome DNA sequencing of over 400 bacterial isolates in a *C. ptb.* collection that had been amassed at UC Davis since 1996 to perform the largest population genomics analysis performed on this pathogen. Genome-based population structure shows two groups corresponding to known subgroup designations equis and ovis, respectively associated with infecting horses and sheep/goats. Surprisingly, there is little genomic diversity within each subgroup, even across years and geography (sampled from USA, mostly California); greater diversity has been seen in other parts of the world with less sampling. With the lack of diversity, no clear associations could be made to the presence of genes or major gene variants to antimicrobial resistance, body location of infection, or opposite host-subgroup infections. Genomic distinction between subgroups is clear, with



Hierarchical relationship tree based genomic similarity (left), animal host species indicator for samples by row (center), and heat map of genomic similarity matrix (right).

shared genes diverging in DNA sequence and each having an exclusive set of ~100 genes. The most notable difference, as previously discovered, is that subgroup equis has a set of nar genes for nitrate/nitrite reduction, enabling high-energy yield metabolism without oxygen as in some deep abscess infections. We confirm that, in our large sample population, the full set of nar genes are present in all subgroup equis samples and that this is part of the equis exclusive set of genes, further supporting it as a marker for diagnostics. Although no antibiotic-specific gene associations were found, we can also confirm there are multiple drug efflux pump systems found in all our samples, each able to act on multiple antibiotics.

How does this research benefit horses? Infections by bacteria species *Corynebacterium pseudotuberculosis* cause "pigeon fever" in horses. Without a commercially available vaccine, isolation of infected animals and insect control remain the primary measures of disease prevention. Whole genome sequencing and bioinformatics innovations allow population comparative genomics that provide innovative solutions to identify new drug and vaccine targets. The results of this study provide a population scale approach to explore genome-based associations to improve approaches to diagnose, treat, and control this organism in animals.

Evaluation of the SarcoFluor antibody test for the detection of antibodies to *Sarcocystis neurona*, agent of equine protozoal myeloencephalitis, in blood and cerebrospinal fluid (Grant #20-9)

Investigators: Pranav Pandit, MPVM, PhD, Patricia Conrad, DVM, PhD, Woutrina Smith, DVM, MPVM, PhD, Monica Aleman, MVZ, PhD, DACVIM (LAIM and Neurology), Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Equine protozoal myeloencephalitis (EPM) is a challenging disease to diagnose in horses with neurological signs. To optimize contemporary diagnostic testing, the SarcoFluor antibody test for *Sarcocystis neurona* was reevaluated using 172 horses diagnosed with EPM and other neurological diseases. When differentiating between EPM and other neurological diseases, the combination of serum and CSF SarcoFluor testing added more information to the model accuracy than either test alone. Utilization of antibody titers against *S. neurona* in serum and CSF result in a high probability in support of EPM in the clinical setting.

How does this research benefit horses? EPM is a diagnosis of exclusion and relies on the presence of neurological signs, ruling out other neurologic disorders, and the detection of antibodies to *S. neurona* in serum and CSF using quantitative immunodiagnostic tests. Accurate diagnostic modalities are needed to prevent over diagnosing or underdiagnosing relevant infectious diseases. The present reevaluation of the SarcoFluor using contemporary samples showed that a diagnosis of EPM can be accurately supported through the antibody testing against *S. neurona* in both serum and CSF. The use of serum to CSF antibody titer ratio against *S. neurona* was not superior to the combination of serum and CSF in support of EPM.

This research was reported in *Vet Parasitol* 2024;:330:110219.

Investigation of the role of horses in the COVID-19 pandemic (Grant #20-12)

Investigators: Emir Hodzic, DVM, PhD, Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Various domestic animals (cats and dogs) and large captive cats (lions, tigers) have been shown to become infected with SARS-CoV-2, often via direct or indirect interaction with clinically or asymptomatically infected humans. The role of companion animals such as cats and dogs are relevant considering the large number of such animals living in close contact with human beings and the many opportunities to acquire, amplify and potentially transmit SARS-CoV-2. While horses have been shown to have the angiotensin converting enzyme II (ACE2) receptor able to bind with the S protein of SARS-CoV-2, there is no available clinical or epidemiological data supporting the role of equids as a reservoir of infection contributing to human-to-human disease, infectivity and community spread. The present study investigated the status of healthy and sick horses regarding SARS-CoV-2. The investigators validated a commercial COVID-19 spike protein ELISA to determine the presence of specific SARS-CoV-2 antibodies in horses at a race venue that was closed after jockeys and track workers tested positive for SARS-CoV-2. The study results showed that amongst 587 racing Thoroughbreds, 35 (5.9%) horses had detectable antibodies to SARS-CoV-2.

How does this research benefit horses? The research focus of the COVID-19 pandemic has understandably been on human health. However, little is known about the role of animals in this pandemic, and we are faced with many urgent questions that can only be answered through investigative studies and surveillance. While horses are apparently susceptible to SARS-CoV-2 and are likely to become infected through spillover from COVID-19 individuals, horses are unlikely to contribute to the spread of SARS-CoV-2. It is, however, important to continue to monitor possible human-to-horse transmission, especially with the emergence of highly transmissible SARS-CoV-2 variants, and to recommend that COVID-19 individuals avoid close contact with companion animals (dogs, cats, ferrets, horses).

This research was reported in *Animals (Basel)* 2022;12(5):614.

Investigation of newly discovered viruses in the nasal secretions of healthy and sick horses (Grant #20-17)

Investigators: Emir Hodzic, DVM, PhD, Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Three novel equine parvoviruses have recently been identified through metagenomics in the plasma and respiratory swabs of 13 horses with unexplained respiratory signs. These viruses are equine parvovirus-hepatitis (EqPV-H), equine parvovirus-CSF (EqPV-CSF) and equine copiparvovirus (Eqcopivirus). No large case-control study has been performed to test for statistically significant associations between the genetically characterized equine viruses and respiratory signs. Nasal fluid samples and blood from 667 equids with acute onset of fever and respiratory signs submitted to a diagnostic laboratory were analyzed for the presence of common equine respiratory pathogens (equine influenza virus, equine herpesvirus-1/-4, equine rhinitis A and B virus, *S. equi* subspecies *equi*) as well as EqPV-H, EqPV-CSF and Eqcopivirus by qPCR. An additional 87 clinically healthy horses served as controls. One hundred and seventeen sick horses tested qPCR-positive for at least one of the three parvoviruses. Co-infections with common respiratory pathogens and parvoviruses were seen in 39 sick equids. All 87 clinically healthy horses tested qPCR-negative for all tested common respiratory pathogens and 10 healthy horses tested qPCR-positive for one of the equine parvoviruses. When the frequency of detection for EqPV-H, EqPV-CSF and Eqcopivirus of equids with respiratory signs was compared to that of clinically healthy horses, the difference was not statistically significant ($p > 0.05$), suggesting that the three recently identified equine parvoviruses do not contribute to the clinical picture of equids with respiratory disease.

How does this research benefit horses? The relative neglect in the investigation of less characterized infectious respiratory pathogens may be related to the dominant position of EIV and EHV-1/-4 as causes of acute upper airway infection in horses, but is also related to a lack of sensitive, widely available and adopted diagnostic tests for less characterized respiratory viral pathogens. The past three decades have seen almost no discovery and characterization of new equine respiratory pathogens, compared to the human medical field. The investigation of less common pathogens and their possible

interaction in co-infection is essential to improve the wellbeing of horses. It is imperative to gain a better epidemiological understanding of recently discovered equine respiratory viruses and to determine their possible association with respiratory disease. While EqPV-H, EqPV-CSF and Eqcopivirus can be found predominantly in the blood of equids with acute onset of fever and respiratory signs, it does not appear that these three newly identified parvoviruses contribute to the clinical picture of equids with respiratory disease.

This research was reported in *Animals* (*Basel*) 2021; 19;11(10):3006.

Is equine oral cancer associated with a virus? (Grant #20-20)

Investigators: Brian Murphy, DVM, PhD

Squamous cell carcinoma (SCC) is one of the most common cancers of the equine oral cavity. Unfortunately, current treatment options for oral SCC are limited, often resulting in a poor prognosis and euthanasia. The cause of this important oral tumor in horses remains unknown. Research has shown that a cancer-associated virus is present in approximately half of the SCC lesions in the equine stomach. Closely related viruses are responsible for cervical cancer in women and are associated with cancer of the oral cavity in people. We suspected that the equine version of this virus, Equus caballus papillomavirus 2 (EcPV2), is associated with equine oral SCC. We performed polymerase chain reaction (PCR) and in-situ hybridization (ISH) for EcPV2 on 31 formalin-fixed paraffin-embedded equine oral SCCs (lingual, gingival, palate) and 10 equine non-SCC oral samples. PCR for EcPV2 was positive in 10/31 (32%) oral SCCs while all non-SCC oral samples were negative. Intense hybridization signals for EcPV2 nucleic acid were detected by ISH within neoplastic epithelial cells in 8/31 (26%) oral SCCs but not in the adjacent normal oral mucosa. No hybridization signals were detected within control samples. This study helps establish a link between EcPV2 and oral carcinoma, the most common oral tumor in horses.

How does this research benefit horses? This study helps establish a link between equine papillomavirus and oral carcinoma, the most common oral tumor in horses. Once causality is understood, improved methods of detection, diagnosis and treatment will follow.

This research was reported in *J Comp Pathol* 2023;205:1-6.

Frequency of detection of a novel EHV-1 genotype (H752) in nasal secretions from horses with acute onset of respiratory disease (Grant #21-B)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Since the full genome sequencing of two prototype EHV-1 strains, Ab4 (neuropathogenic) and V592 (non-neuropathogenic), most diagnostic laboratories in the USA rely on allelic discrimination qPCR assays to detect EHV-1. Unfortunately, such a molecular approach may lead to missed EHV-1 cases as exemplified by recent outbreaks from Europe and the USA. With the discovery of a new H752 genotype of EHV-1 and the validation of a SNP discriminatory assay, every EHV-1 infection can be successfully attributed to one of three genotypes. A total of 297 EHV-1 qPCR-positive swabs collected from 2019 to 2022 from horses with respiratory disease (EHV-1), neurological disease (equine herpesvirus-1 myeloencephalopathy (EHM)) and

abortion were tested for the three different EHV-1 genotypes (N752, D752 and H752) using qPCR allelic discrimination assays. All submissions originated from the USA and included 257 EHV-1 cases, 35 EHM cases and 5 cases of abortion. EHV-1 qPCR-positive cases were predominantly seen during winter and spring. N752 was the predominant genotype detected in EHV-1 cases (87.5%), EHM cases (74.3%) and abortions (80%). D752 was detected less frequently in EHV-1 cases (9.3%) and EHM cases (25.7%), while H752 was only detected in EHV-1 cases (3.1%).

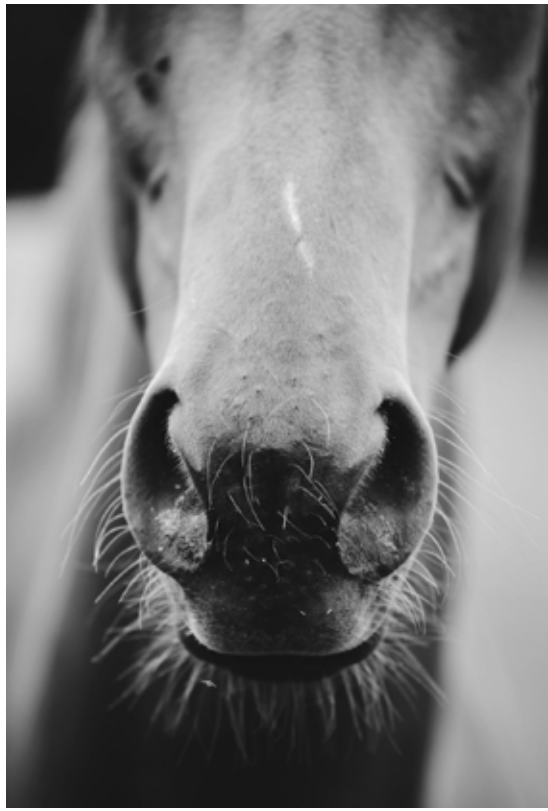
How does this research benefit horses? While the N752 genotype has remained the predominant genotype affecting horses with respiratory disease and abortion, it has also become a leading genotype in cases of EHM, when compared to historical data. The new H752 genotype, first reported in the United States in 2021, has remained confined to a cluster of geographically and temporally related outbreaks and the data showed no emerging spread of H752 since it was first reported. While the monitoring of EHV-1 genotypes is important from a diagnostic and epidemiological standpoint, it may also help establish medical interventions and preventive protocols to reduce the risk of severe complications associated with EHV-1 infection.

This research was reported in *J Equine Vet Sci.* 2023;123:104244.

Investigation of the antibody response and antigen detection against EHV-1 following the intranasal administration of two commercially available EHV-1 vaccines (Grant #21-C)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Two EHV-1 vaccines are routinely used intranasally, especially in high-risk horses and outbreak situations. One of these vaccines is a killed-adjuvanted EHV-1 vaccine (Calvenza-EHV, Boehringer Ingelheim Animal Health), labeled for intramuscular and intranasal administration. The second vaccine is a modified-live EHV-1 vaccine (Rhinomune, Boehringer Ingelheim Animal Health), labeled for intramuscular administration. For this study, the investigators enrolled 30 healthy adult horses with no recent EHV-1 vaccination. The horses were randomly allocated to one of three groups: (i) Rhinomune intranasal vaccine group, (ii) Calvenza-EHV intranasal vaccine group, and (iii) Control group. Prior to vaccine administration and daily thereafter for 7 days, nasal secretions were collected for the detection of EHV-1 via qPCR. Further, whole blood was collected on the day of vaccine administration and 30 days later for antibody detection using an EHV-1 specific ELISA. Vaccine-derived EHV-1 was only detected in the two EHV-1 vaccine groups with 9/10 horses in the Rhinomune group and 8/10 horses in the Calvenza group testing qPCR-positive for EHV-1 for 1 to 4 days. Total Ig and isotype-specific IgG4/7 against EHV-1 measured pre- and 30-days post-vaccination were not different amongst the three study groups.



How does this research benefit horses? The main benefit of this study was to determine how long vaccine-derived EHV-1 could be detected in nasal secretions following intranasal administration. This is relevant information as vaccine-derived antigen and naturally occurring EHV-1 are not routinely differentiated using molecular diagnostic tools. Vaccine derived EHV-1 could be detected in most of the intranasally vaccinated horses up to 4-days post-vaccine administration, potentially affecting diagnostic interpretation of EHV-1 during outbreak situations. A second benefit of this study was to determine if intranasally administered EHV-1 vaccines could induce a measurable antibody response to EHV-1. Unfortunately, the intranasally administered commercial EHV-1 vaccines did not elicit a systemic immune response. Therefore, this vaccine route seems suboptimal and should not be used to vaccinate adult horses during and outside an EHV-1 outbreak.

This research was reported in *J Equine Vet Sci.* 2023;122:104229 and Viruses 2024;16(7):1070.

Investigation of neurological outbreaks of herpesvirus-1 (Grant #21-I)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Recent outbreaks of equine herpesvirus-1 myeloencephalopathy (EHM) around the world have highlighted the complexity of controlling the spread of EHV-1 and determining the infection state of exposed horses. Further, every well-investigated outbreak has added valuable information regarding the virus, the affected population, the clinical presentation, and the efficacy of specific preventive and therapeutic strategies. However, most EHM outbreaks remain poorly investigated mainly because of the laboratory costs associated with horse testing. The present study aimed at investigating a contemporary outbreak of EHM caused by the novel genotype H752. The morbidity of the EHV-1 outbreak was 84% with 26 clinically infected horses displaying fever, and less frequently anorexia and swelling of the hind limbs. Four horses showed mild transient neurological deficits. Clinically diseased horses experienced high viral load of EHV-1 in blood and/or nasal secretions via qPCR, while subclinically infected horses had detectable EHV-1 mainly in nasal secretions. Most infected horses showed a rise in antibody titers to EHV-1 during the outbreak. All 31 horses were treated with valacyclovir, while clinically infected horses further received flunixin meglumine and sodium heparin.

How does this research benefit horses? This study aimed at investigating an unusual contemporary outbreak of EHM by supporting laboratory analysis (molecular and serological testing) and by collecting demographic, clinical and laboratory information. This investigation highlights various relevant aspects of an EHV-1 outbreak caused by a new H752 genotype: (i) importance of early detection of EHV-1 infection; (ii) diagnostic challenge to assess H752 genotype; (iii) apparent benefit of valacyclovir use in the early stage of the outbreak; and (iv) weekly testing of blood and nasal secretions by qPCR to monitor individual infection status and lift quarantine.

This research was reported in *Pathogens* 2021;10(6):747.

Full genome sequencing of EHV-1 strains associated with recent outbreaks (Grant #21-U)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, Daniel Rejmanek, Beate Crossley, DVM, MPVM, PhD, Beatriz Martinez Lopez, DVM, MPVM, PhD, Shadira Gordon, DVM, MPVMc

Current research suggests a multifaceted interplay between viral genetics, host characteristics, and environmental factors in the development of equine herpesvirus-1 myeloencephalopathy (EHM). While specific gene deletions and mutations have been identified, their association with disease severity remains unclear. Additionally, the influence of host characteristics such as age, breed, and vaccination status on EHM development requires further elucidation. Understanding these factors is crucial for developing targeted interventions and preventive strategies. A total of 22 isolated EHV-1 positive samples detected by PCR performed on nasopharyngeal swabs and blood samples were obtained from the California Department of Food and Agriculture (CDFA) during outbreaks from 2022-2023. The isolated samples were characterized by allelic-discrimination analysis for seven single-nucleotide polymorphisms (SNPs) within the open reading frames (ORFs) 30, 33, and 72, which are genes known to have the greatest level of divergence among EHV-1 strains. EHV-1 DNA was sequenced in collaboration with colleagues from the California Animal Health & Food Safety Laboratory (CAHFS). Various SNPs were identified among the different EHV-1 isolates and associated with disease form (respiratory versus EHM). Further, direct or indirect relationships between the various outbreaks could be established by homology of the various SNPs. The established genomic patterns of the three targeted EHV-1 genes were associated with disease outcome and allowed us to establish relationships between the various outbreaks.

How does this research benefit horses? One key aspect of this research lies in its potential to advance ongoing genomic surveillance efforts. This not only aids in the early detection of EHM outbreaks but also enables the identification of emerging trends, novel genetic variants, and potential outbreak clusters. The identification of genetic markers and future analysis of transmission networks can help develop risk assessment tools tailored to specific events and equine populations. In addition to enhancing disease surveillance and risk management, this research also has significant implications for vaccination protocols. After

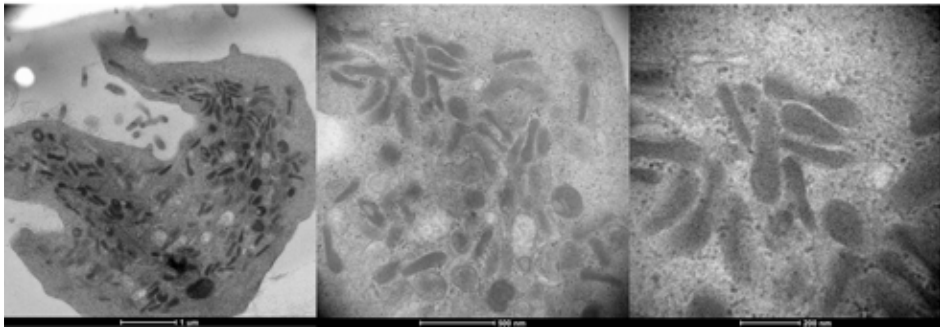
understanding the specific genetic markers and host characteristics associated with EHM susceptibility, vaccination strategies can be tailored to individual horses or vulnerable populations.

ORTHOPEDICS & LAMENESS

Mitotherapy for equine joint disease: evaluating mitochondria's potential to treat joint inflammation and prevent osteoarthritis (Grant #19-02)

Investigators: Jennifer Cassano, DVM, PhD, Krzysztof Marycz, PhD, Natalia Vapniarsky-Arzi, DVM, PhD, DACVP

Inflammation of the lining of the joint (synovitis) is a key factor in the development of osteoarthritis, which contributes to 60% of lameness in horses. In our study, a mild synovitis was induced in the left and right knee joints of 6 horses by injecting lipopolysaccharide (bacterial cell wall component). Mitochondria isolated from each horse's own blood was injected into the right joint. The horses tolerated this well, with no signs of inflammation. There was no change in general physical exam parameters after injecting mitochondria or the control. Total white blood cell counts from peripheral blood remained stable throughout the study. Synovial fluid cell counts increased following the induction of synovitis with lipopolysaccharide, indicating the induced synovitis model was working as expected. There was significant variation in numerous cytokines over time, with inflammatory markers peaking at 8 hours. Gene expression analysis of synovial fluid cells and microRNA library preparation are in progress. If a biomarker is found in response to mitochondria treatment, the next step will be to evaluate the benefit of mitochondria in naturally occurring osteoarthritis.



Transmission electron microscopy images of mitochondrial fraction isolated at increasing magnifications, with the typical kidney bean shape of mitochondria readily visible.

How does this research benefit horses? Synovitis and osteoarthritis are common clinical problems in horses and exert a significant economic burden on the equine industry. In this study, we expanded our knowledge of a commonly used equine model for synovitis and evaluated a novel therapy using mitochondria, which has the potential to restore synovial cells' anti-oxidative defense and reduce their pro-inflammatory activity, halting the progression of synovitis to osteoarthritis.

Promoting tendon formation through the inhibition of glycolysis (Grant #19-10)

Investigators: Michael Mienaltowski, DVM, PhD

Previous studies demonstrated that slowing down glycolysis reduced scar formation and inappropriate cartilage formation for progenitor cells from injured human tendons. In this study, we used 2-Deoxy-D-glucose to inhibit glycolysis in tendon proper and peritenon progenitors grown in three-dimensional tendon constructs – an in vitro tendon formation model. Glycolysis inhibition was shown early on to promote transcription factors that encourage tendon differentiation. Glycolysis inhibition also slowed down collagen synthesis in equine superficial digital flexor tendon progenitor cells, while promoting the expression of other collagen regulatory molecules that work to better organize the collagen in tendon. From this in vitro study, it seems that modulation of glycolysis could ultimately lead to improved tendon repair in horses, suggesting potential for glycolysis inhibition as a strategy to aid in tendon repair. We are working on the development of further mechanistic follow-up studies to optimize concentrations and timing of the use of this inhibitor to improve outcomes for the cellular responses.

How does this research benefit horses? The study demonstrated the promise of using the 2-deoxy-d-glucose sugar molecule to reduce imperfections

like scar formation within the culture model. Further optimization is required, but the goal is to ultimately consider how conservative use of such an affordable sugar could be used to promote tendon repair.

Which equine muscles are important for jumping?

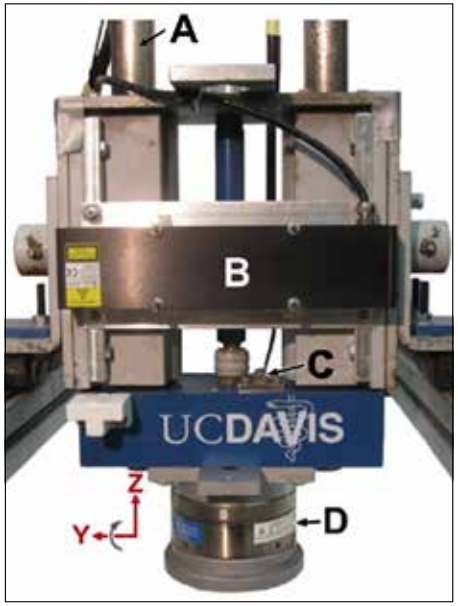
(Grant #20-3)

Investigators: Christina Rohlf, PhD, David Hawkins, PhD, Tanya Garcia, MS, Susan Stover, DVM, PhD, DACVS

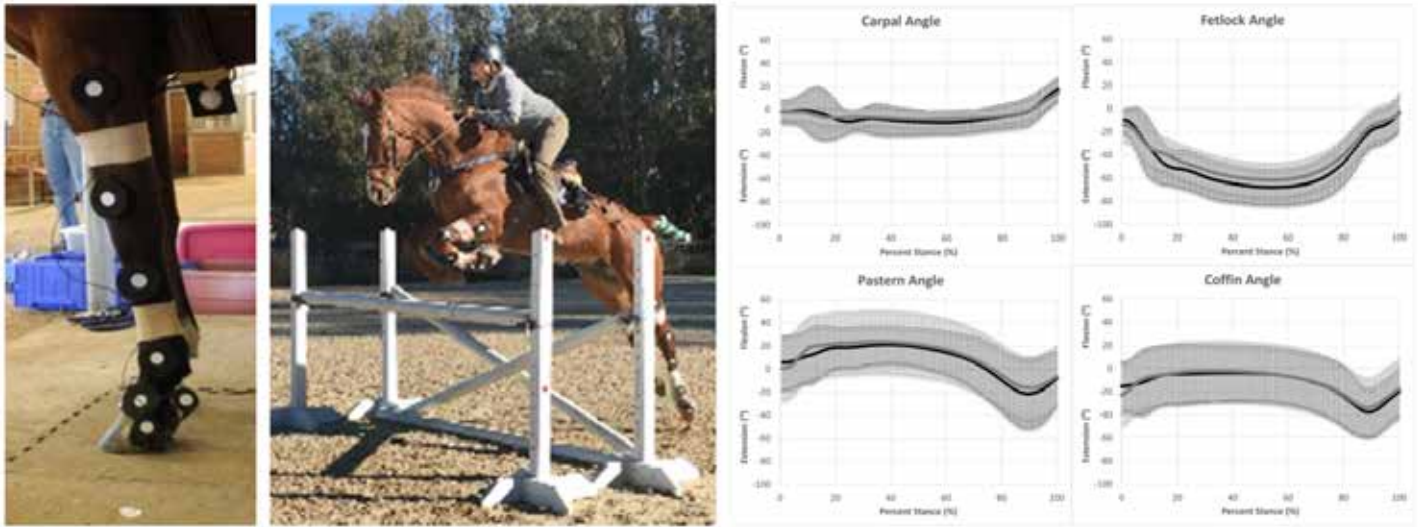
Show jumping horses commonly injure tendons and ligaments in the lower limb. To identify factors associated with the risk of injury, it is important to know how jumping loads are distributed between muscles and tendons. Although muscle forces cannot be measured directly in jumping horses, computer modeling techniques can be used to determine muscle activity. This requires two inputs: associated lower limb motions and ground reaction forces (GRFs) for the same jumping trial. Lower limb motions were collected from 4 horses during trotting and jumping on 12 different arena surfaces (5 dirt, 7 synthetic) using marker-based video capture. Ground reaction forces were collected indirectly with a surface tester. We chose to indirectly measure GRFs, because direct measures of GRF may affect natural movement by imposing additional weight on the hoof (force sensing horseshoe) or by altering the surface (force plate). GRFs as measured by the surface tester were fit to an established surface mathematical model and extrapolated to hoof GRFs using measurements of hoof displacement and velocity. However, the magnitude of GRFs was 2-3x higher than the 7-9kN expected at jump landing when using this method. Our findings suggest that future work into the development of a direct method of GRF measurement that does not alter natural locomotion is a necessary step toward building a computer model to evaluate equine muscle activity.

How does this research benefit horses? These results suggest a possible direction of further research to understand equine biomechanics during show jumping and continue the development of a dynamic computer model. Recent developments such as pressure sensitive fabrics and micro-scale sensors show promise for the development of a novel force sensitive device attached to the hoof.

This research was reported in *Animals* 2023;13(13):2122.



Vertical impact surface testing device.



Carpal, fetlock, pastern, and coffin joint angular changes during jumping as measured with video capture.

Supplementing vitamin C to promote tendon formation (Grant #20-7)

Investigators: Michael Mienaltowski, DVM, PhD

Horse tendinopathy greatly impacts the well-being and performance of horses of all breeds and uses. There is great value in the development of novel therapeutic strategies to improve repair responses for tendon injuries. In this study, we examined the impacts of vitamin C supplementation on cells collected from within the superficial digital flexor tendon and those along the outside of the tendon of horses - both of which are essential to proper tendon function. We found that vitamin C had several roles in promoting tendon formation, including bolstering anti-inflammatory proteins while inhibiting pro-inflammatory proteins, preventing tendon calcification (which structurally weakens tendon), and promoting matrix assembly. In some instances, there were increases in collagen synthesized, which is helpful for forming new strong tendon. Finally, vitamin C could protect tendon cells from cell death caused by corticosteroid exposure. These findings offer promising results that indicate that vitamin C should be further considered in therapeutic strategies. Follow-up studies will focus on understanding the role of vitamin C in protecting tendon cells against adverse effect of other drugs used with tendinopathy and in how best to deliver vitamin C locally to affected sites.

How does this research benefit horses? Our studies demonstrate the potential for supplemental vitamin C to promote tendon formation in tendon proper and peritenon cells. By working from multiple approaches, this affordable biomolecule could potentially be added to injury sites or sites of tendinopathy for a positive outcome. While this is an in vitro study, the promising results will lead our group to design studies in which vitamin C could be added to tendinopathy treatments.

PET imaging of the racehorse fetlock after surgical repair of fracture (Grant #20-10)

Investigators: Mathieu Spriet, DVM, MS, DACVR, DECVDI, DACVR-EDI, Thomas Bergstrom, DVM, Ryan Carpenter, DVM, MS, DACVS-LA

Fractures of the cannon bone are common in racehorses, but novel imaging may help prevent them by detecting early signs. Fourteen horses that had sustained a surgically repaired fracture of the cannon bone were imaged with Positron Emission Tomography (PET) to understand the changes that led to the fracture and to see how fractures heal over time. Both the fractured limb and the other limb were imaged up to 3 times - immediately after fracture repair, 3 months later and 5 months later. The scans demonstrated that there were associated findings that preceded fractures based on imaging of the non-fractured limbs. The fractured limbs demonstrated a specific pattern with evidence of altered stress on the limb, with more stress on the outside than the inside, which is likely to contribute to the fracture. PET also confirmed healing of most of the fracture by 3 months; however, a few fractures had evidence of delayed healing on PET scans, leading to delay or inability to resume racing. Complications from the fracture with development of degenerative changes could also be detected with PET scans.

How does this research benefit horses? This study confirmed the value of PET to recognize horses at risk for fracture and potentially prevent the fractures by modifying the training and racing program. PET was also useful post fracture repair to guide rehabilitation and predict ability to resume racing.

This research was reported in *Vet Surg* 2024;53(1):131-142.

Calibrating a model of racehorse proximal sesamoid bone stress fractures for injury prevention (Grant #21-L)

Investigators: Sarah K. Shaffer, PhD, Susan Stover, DVM, PhD, DACVS, David P. Fyhrie, PhD

Fracture of the proximal sesamoid bones (PSBs) is the most common fracture in Thoroughbred racehorses. PSB fracture is related to the presence of focal subchondral bone lesions (regions of abnormally porous, damaged bone beneath the articular surface). Importantly, lesion severity is associated with training intensity. However, it is difficult to predict how training causes lesion formation because bone responds to both mechanical loading and damage. The goal of this study was to perform an initial calibration of a compartment model of bone turnover.

First, we derived steady-state rate constants for a compartment model

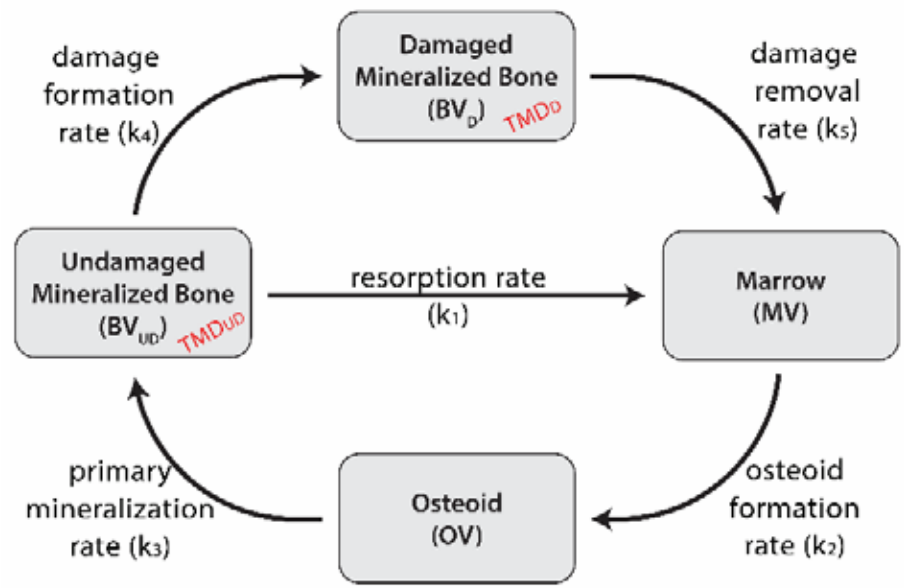


Figure 1

of bone's tissue turnover cycle using data from fractured and non-fractured racehorse proximal sesamoid bones (Figure 1). Model rate constants were determined in two regions: the lesion and a control region. Second, these rate constants were related to high-speed training history.

Steady-state rate constants were determined using bone volume fraction, tissue mineral density, and microdamage area fraction measurements. We were unable to collect data on newly formed bone due to the prevalence of damaged tissue at the lesion site. To solve the model at steady state, we assumed a fixed primary mineralization rate (k3) and derived a relationship for tissue mineral density (TMD) based on literature. In horses, k3 is unknown; however, in other species, there is limited evidence it is affected by mechanical loading (unlike the other model rate constants). Our results indicate the choice of k3 did not affect the relationships observed between other rate constants and exercise.

The derived undamaged bone resorption rate, damage formation rate, and osteoid formation rate had significant robust regression relationships to exercise intensity (rate) variables, layup (time out of exercise), and exercise 2-10 months before death. The direction of these relationships varied between the stress reaction and non-damaged regions, reflecting that the biological response to damage differs from the response to changes in non-damaging exercise.

How does this research benefit horses? We are developing a computer model to determine how existing and novel horse training programs influence lesion formation and, therefore, PSB fracture risk. This study provided an initial calibration of a compartment model of bone turnover in racehorses that can help us make these predictions. The compartment model allows observable measures in bone (e.g., damaged mineralized bone) to be related to exercise history. To link this model with a computer program capable of predicting lesion formation under different training programs, we first needed to establish if and how model rate constants could be related to exercise. Under steady-state conditions (e.g., a habitual training program), observed relationships between model rate constants and exercise differed based on if they were found in a damaged or control region. These relationships are consistent with bone biology. In the future, these relationships could be used to dynamically drive the rate constants with strain (or another exercise-related parameter) in a finite element model capable of predicting lesion formation under virtual training conditions.

This research was reported in *Sci Rep* 2023;13:205.

REPRODUCTION

Evaluation of the use of different treatments to control uterine inflammation after breeding (Grant #18-24)

Investigators: Ghislaine A. Dujovne, DVM, MS, DACT, Daniela Orellana-Guerrero, DVM, MS, DACT, Eduardo Santos -Villanueva, DVM, DACT, Elizabeth Scholtz, DVM, DACT, Pouya Dini, DVM, PhD, PhD, DACT, DECAR

Breeding induced endometritis is one of the leading causes of infertility. Several treatments are used and controlled studies are necessary to establish the best treatment for use in older mares and mares susceptible to persistent endometritis. In this study, mares who are susceptible to persistent breeding induced endometritis were treated with either systematic dexamethasone or intrauterine

platelet rich plasma. While there was no difference in inflammation or pregnancy success with either treatment, an expanded understanding of how these treatments work was identified using a molecular technique (endometrial transcriptome).

How does this research benefit horses? The information obtained in this study helps us understand the response of the uterus (endometrium) at the molecular level to the use of systemic dexamethasone and intrauterine platelet rich plasma to better understand their mechanism of action. This knowledge helps to develop and determine the most appropriate treatments for endometritis post-breeding.

Understanding the interaction between the bacteria and placenta during equine nocardioform placentitis (Grant #20-4)

Investigators: Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Bart Weimer, PhD, Margo Verstraete, DVM, Machteld van Heule, DVM

Nocardioform placentitis is a disease affecting pregnant horses, usually in the later stages of pregnancy. Several studies have reported nocardioform placentitis in various states and countries, dispelling the belief that this condition is limited to central Kentucky. This condition is associated with certain types of bacteria that have a characteristic appearance under the microscope. They are ″filamentous″ and ″branching″ and stain positively in a Gram stain, a common way to classify bacteria. The main types of bacteria connected with this disease are *Crossiella equi, Amycolatopsis spp*., and *Streptomyces spp*. Despite this, not all horses with the disease have these bacteria, and sometimes these bacteria are found in the placentas of healthy horses after they have given birth. To better understand this condition, we worked with veterinary clinics and practitioners to collect placental samples. We then examined the diversity of microbes present in the placenta of both healthy and disease-affected horses. Our analysis indicates that there could be a wider range of bacteria that might contribute to the disease than previously thought. These bacteria could lead to changes in the placenta's tissue structure that look like those caused by the traditionally recognized bacteria associated with nocardioform placentitis. This information led us to start investigating this disease based on the activity of the microbes.

How does this research benefit horses? Our research demonstrated that the condition known as nocardioform placentitis is associated with a broader range of microbes than previously recognized. This variability may explain the inconsistent efficacy of treatments observed in clinical cases. Our findings underscore the complexity of nocardioform placentitis and emphasize the need to identify the specific underlying cause of the disease prior to initiating antibiotic therapy.

This research was reported in *Theriogenology* 2023;206:60-70; J Vet Eq Sci 2023;125: 104789

Regulation of gene expression in the equine placenta; what makes the placenta function? (Grant #20-13)

Investigators: Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Carrie J. Finno, DVM, PhD, DACVIM (LAIM), Margo Verstraete, DVM, Daniela Orellana-Guerrero, DVM, MS, DACT

The placenta is a vital organ during pregnancy, impacting the long-term health of both the foal and the dam. The placenta works by changing its gene activity at different stages of pregnancy. Our study explored these changes by examining DNA methylation in horse placentas, which is a key process influencing gene activity. We analyzed placenta samples at four, six, and ten months of gestation to track how DNA methylation patterns evolve. We found that, as pregnancy progresses, the placenta's DNA becomes more methylated. By comparing gene activity data with our methylation findings, we pinpointed genes that were turned up or down in relation to methylation levels at various stages. Our results showed that these changes mainly control important functions like cell movement, blood vessel formation, and the processing of vital nutrients. Among the identified genes, *Fibrillin 2* (*FBN2*) stood out as it is known to produce placensin (a hormone critical for glucose management during pregnancy) in humans. Since glucose is the primary energy source for the fetus, and changes in glucose and insulin resistance levels are documented in horses, our findings hint at *FBN2*'s potential role in equine gluconeogenesis. Understanding the expression of *FBN2* in the equine placenta and the levels of placensin in the mare's blood may shed light on glucose homeostasis in pregnant mares. Exploring this further could reveal how alterations in maternal glucose

and insulin might affect fetal development—a phenomenon well documented in humans. This was the first detailed study of how DNA methylation in horse placentas changes throughout pregnancy, providing a basis for future research into how deviations from this pattern could affect pregnancy outcomes.

How does this research benefit horses? By understanding the normal methylation patterns during pregnancy, breeders can potentially identify deviations that may predict complications, allowing for early interventions.

This research was reported in *Int J Mol Sci* 2023;24(8):7084 and *J Eq Vet Sci* 2023;125:104778.

Gene expression of equine cumulus cells during oocyte maturation: in vitro and in vivo conditions

(Grant #20-14)

Investigators: Stuart Meyers, DVM, PhD, DACT, Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Ghislaine A. Dujovne, DVM, MS, DACT

Assisted reproductive techniques (ART), including *in vitro* embryo production, have become important tools for the successful breeding of mares. These include normal mares and mares that cannot conceive by other natural means, or mating to deceased or unavailable stallions that possess a reduced cryopreserved semen bank or have inherent low sperm quality. Retrieval of immature oocytes represents an important tool in achieving this goal; however, *in vitro* matured oocytes have not been optimized, while *in vivo* matured oocytes have shown a better maturation rate and developmental competence. In this study, we determined differences in the gene expression of cumulus cells (cells that surround oocytes and play critical roles in oocyte maturation) of those cumulus-oocyte complexes (COCs) matured *in vivo* and those matured *in vitro* using RNA sequencing which could reveal insights into oocyte maturation and fertility. We also aimed to relate these gene expression profiles to the cellular morphologies of the oocyte and the cumulus expansion rate in order to increase our understanding of equine oocyte maturation and improve the existing maturation conditions.

How does this research benefit horses? *In vitro* production of embryos is an important and growing tool in the equine breeding industry and is crucial in mares that cannot conceive by other means. This study will help to understand the differences between *in vivo* and *in vitro* maturation processes and serve to optimize production of high-quality embryos.

This research was reported in *J Eq Vet Sci* 2022;113:103963 and *Reprod Fertil Devel* 2023;35:242-243.

Can cumulus cells during in vitro maturation predict successful fertilization and embryo development in horses? (Grant #20-19)

Investigators: Stuart Meyers, DVM, PhD, DACT, Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Ghislaine A. Dujovne, DVM, MS, DACT

Cumulus cells surround the oocyte and play an essential role in the processes of oocyte maturation and readiness for fertilization. This study aimed to test our ability to predict fertilization and embryo development before *in vitro* fertilization based on the quality of the cumulus cells. This is a continuation of our study to understand equine embryo development using a non-invasive time-lapse imaging system. Previously, we proposed to track pronuclear formation to predict the first mitotic division in real-time. We were able to visualize some of the structural changes in the zygote prior to the first division, allowing us to predict fertilization outcome in the early stages of embryogenesis. In this study, our goal was to assess the oocyte milieu, including its surrounding cells, during maturation to understand its effect on post-fertilization events and embryo development. We performed RNA sequencing studies to examine immature and *in vitro* matured equine oocytes for gene expression and morphological changes that could be detected in our time-lapse imaging system during the maturation process of equine oocytes.

How does this research benefit horses? By developing a new understanding of the influence of cumulus cells on embryo development and quality, we can optimize production of high-quality embryos from valuable mares. Our findings will provide horse breeders and researchers with new methods for successful equine reproduction, with strong application to clinical management of mare subfertility.

This research was reported in *Int J Mol Sci* 2023;24(18):13718.

Assessment of bone growth in horse fetuses and newborn Warmblood foals (Grant #20-21)

Investigators: Catherine Renaudin, DVM, DECAR, Mathieu Spriet, DVM, MS, DACVR, DECVDI, DACVR-EDI, Fiona Wensley, BVM&S, MRCVS, Jessica Morgan, DVM, PhD, DACVSMR, Jennifer Cassano, DVM, PhD

Ultrasonographic evaluation of the first phalanx (P1) has been successfully evaluated in Quarter Horses (QH) and

can be used to assess fetal growth and bone development late in gestation. This study aimed to evaluate the first phalanx (P1) in Warmbloods (WB). The length of P1 was measured. P1 bone maturation was described by recording the time of appearance and closure of P1 secondary ossification centers. Correlation between ultrasonographic findings was observed within the last 2 weeks of gestation and radiographic findings obtained at birth were evaluated. Data was obtained from 9 healthy Warmblood mares with known gestation dates that were ultrasounded transrectally every 2 weeks from 9 months of gestation until parturition. Within 48 hours of birth, radiographs of each foal's lower limb were taken. We found that P1 could be imaged in most examinations and that P1 length was strongly correlated with days of gestation. The proximal and distal ossification centers both appeared between 268 and 298 days of gestation. The proximal ossification center did not close as opposed to the distal one that closed between 306 and 333 days of gestation. Ultrasound findings were confirmed on radiographs except for the length of P1. As P1 becomes too long to be measured close to parturition, the last ultrasonographic measurement is therefore underestimated. The results are very similar to those obtained in QHs.

How does this research benefit horses? We confirm that P1 length can be used as a fetal growth parameter in Warmbloods. In addition to the other growth parameters already known, P1 length will improve prediction of unknown due dates in late pregnancy and the prediction of fetal growth when due date is known. The presence or absence of P1 ossification centers can serve as markers of bone maturation in Warmblood horses that may be used in the future in the decision-making process of inducing parturition in the mare. It may also help identify risk of foal health issues at birth, such as prematurity or dysmaturity, due to abnormal development.

This research was reported in *J Eq Vet Sci* 2023;125:104781.

Equine cumulus cell culture: an in vitro model to study equine oocyte maturation (21-0)

Investigators: Stuart Meyers, DVM, PhD, DACT, Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Alan Conley, BVSc, MS, PhD, FRCVS, DACT, Janet Roser, MS, PhD

In vitro maturation (IVM) of oocytes is an important step of in vitro embryo production (IVP), preparing oocytes for fertilization via intracytoplasmic sperm injection. However, IVM is a limiting step since only a few oocytes typically mature and are available for fertilization. Unfortunately, IVM studies that aim to optimize maturation culture conditions in the horse are limited by the low number of oocytes obtained due to the difficulties of retrieving cumulus oocyte complexes (COCs) from live mares. An important component of COCs that play a critical role during maturation is the cumulus cell layer surrounding the oocyte. These cells provide a niche with important molecules and metabolites that help the oocyte become an embryo. In this study, we aimed to establish and characterize a primary cell culture of equine cumulus cells (CC) obtained from COCs. Our goal is to utilize the CC culture as a valuable and useful model for IVM studies in equine oocytes. Based on our long-term cultures of immature and mature cumulus, it appears that they are unable to be cultured for longer than 2 months, which is logical since *in vivo* cumulus cells are typically only present short-term. Cumulus cells also die after the oocyte resumes meiosis, so it makes sense that cumulus cells cannot be successfully cultured for longer than 2 months. Morphologically, we observed subtle differences in immature and mature cumulus cells. The immature cells are more cuboidal with large cytoplasms, while the mature cells are thinner and more fibroblastic. However, as the immature cells are passaged, they become more fibroblastic in shape and look similar to the mature cells. Because of this, it is possible that the cumulus cells that have grown long term will display abnormal metabolism and behavior. As a result, we have elected to modify our methods. Studies are ongoing to further understand equine cumulus expansion.

How does this research benefit horses? Availability of COCs is the limiting factor to meticulously study the effectiveness of equine oocyte IVM conditions and embryo development. Our goal is to establish a functional primary equine cumulus cell culture model for advanced studies of oocyte IVM and media optimization, thereby reducing the need to perform transvaginal aspiration of COCs.

This research was reported in *J Eq Vet Sci* 2022;113:103963 and *Int J Mol Sci* 2023;24(18):13718.

Selection and characterization of high-quality stallion sperm using microfluidics and sperm cell membrane charge (Grant #21-P)

Investigators: Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Stuart Meyers, DVM, PhD, DACT, Morgan Orsolini, MS

Intracytoplasmic sperm injection (ICSI) is currently the sole clinical technique for producing horse embryos in a lab setting. The success of this process depends heavily on the quality of the sperm used. In human fertility treatments, a property called zeta potential (ZP), which measures the electric charge on the sperm surface, has been linked to sperm health and the success of creating embryos. It was unknown whether this is also true for horse sperm. In this study, we measured the ZP of horse sperm to see if it relates to sperm quality. We also compared traditional sperm sorting methods to a new technique that uses a microfluidic chip. We looked at fresh and chilled sperm samples and tested their motility, viability, and normal shape both before and after sorting them with different methods. We found that horse sperm has a net negative ZP, much like human sperm, and this negative charge is associated with how well the sperm moves and survives. Interestingly, the microfluidic chip was especially good at selecting high-quality sperm without the damage that can be caused by other methods. This study shows that horse sperm has a net negative electric charge that could predict its quality and that the microfluidic chip is a promising new tool for selecting the best sperm for creating horse embryos.

How does this research benefit horses? The optimization and application of microfluidic devices in the selection of equine sperm represent significant technological advancements in horse breeding. This innovation, which we fine-tuned for practical use in clinical settings, offers a superior method of sperm selection. Its increased adoption is a testament to its effectiveness, promising to enhance the success rates of *in vitro* embryo production.

This research was reported in *Theriogenol* 2022;192:1-8, *Animals* 2021;11(11):3248 and 3319, *J Eq Vet Sci* 2022;113:103966.

Mechanisms of placental blood vessel formation in cloned equine pregnancies (Grant #21-R)

Investigators: Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Stuart Meyers, DVM, PhD, DACT, Margo Verstraete, DVM

Somatic cell nuclear transfer (SCNT), or "cloning," enables production of offspring from horses regardless of reproductive status, age, health status, as well as post-mortem. Despite significant technical progress, the overall success of horse cloning is still low and placental abnormalities have been associated with pregnancy failures and decreased survival rates of cloned foals. The most common placental abnormalities in cloned pregnancies include abnormal blood vessel formation, excessive edema, and excessive accumulation of fluid (hydrops). We previously identified a gene that is essential for normal placental blood vessel formation in horses and demonstrated that abnormal expression of this gene is associated with hydrops. The current study evaluated gene expression and DNA methylation of placental samples from cloned equine pregnancies with different outcomes. The results highlight the underlying molecular pathways associated with abnormal placental development in cloned equine fetuses. Moreover, the data demonstrated the disruption of angiogenesis in the cloned placenta, manifested as excessive edema. Similarly, in a previous study, we demonstrated the association between abnormal angiogenesis and placental edema and hydrallantois in equine pregnancy, highlighting the importance of adequate angiogenesis in placental function.

How does this research benefit horses? This research sheds light on the probable causes of the high incidence of pregnancy abnormalities arising from equine somatic cell nuclear transfers, a method used in cloning. Through our studies, we have been able to pinpoint factors that could lead to these complications, providing a foundation for improving cloning techniques and outcomes in horses.

This research was reported in *J Eq Vet Sci* 2022;113:103983.

Equine placentitis: a new approach to understand an old problem (Grant #21-S)

Investigators: Pouya Dini, DVM, PhD, PhD, DACT, DECAR, Bart Weimer, PhD, Fabio Lima, DVM, PhD, Machteld van Heule, DVM

Ascending placental infections and subsequent placental inflammation (ascending placentitis) are among the most common problems of late gestation in mares. Although placentitis is one of the costliest diseases in the equine breeding industry, the exact cause of the disease is not fully understood, leading to inefficient preventive, diagnostic, and treatment protocols. Previously, we characterized the molecular changes in placental tissue at the final stage of this condition. In the current study, we delved into the specific small molecules and virulence factors (VFs) produced by the bacteria involved in this condition. We identified 20 genes linked to virulence that are active in diseased placental samples but not active in healthy placentas. This breakthrough paves the way for refining diagnostic methods and, ultimately, treatment strategies for placentitis. By applying this knowledge, we aim to decrease the rates of pregnancy loss and the economic impact associated with this disease in the equine industry.

How does this research benefit horses? This research will lead to identifying better diagnostic tools for equine placentitis. The resulting insights will be used to optimize diagnosis and treatment, and consequently lower pregnancy loss rates and financial loss in the equine breeding industry.

SPORTS MEDICINE

How common are abnormal heart rhythms in horses, and which horses are at risk? (Grant #20-25)

Investigators: Jessica Morgan, DVM, PhD, DACVSMR, Joshua Stern, DVM, PhD, DACVIM, Ashley Hill, DVM, MPVM, PhD

Electrical disturbances in the heart, known as cardiac arrythmias, are common in horses. While some of these electrical disturbances are considered normal, others are not. In some cases, abnormal electrical disturbances can be problematic and associated with decreased performance, collapse, or sudden death. More information is needed about frequency of arrhythmias in normal horses to be able to make recommendations regarding safety and risk of future cardiac events. We recorded electrical activity of the heart over a 24-hour period on 98 horses from a mixed breed population with a mean age of 12 years. Abnormal rhythms were present in 91.8% (90/98) of horses, with 22.4% (22/98) of those horses having more than one arrythmia per hour of recording. Of the horses that had arrhythmias, 94.4% (85/90) had supraventricular arrhythmias (premature beats that occur prior to the expected beat) and 25.5% (23/90) had ventricular arrhythmias (concerning electrical disturbances in the lower chambers of the heart). While preliminary analysis found no significant relationships between number of arrythmias and age, weight, troponin values, body condition score, or heart girth circumference, there was a trend for a greater number of arrythmias in horses with a higher body condition score. This data will be made available for future studies looking for risk factors for cardiac arrhythmias as more information about these horses is discovered through ongoing work in the Pioneer 100 Horse Health Project.

How does this research benefit horses? Abnormal heart rhythms can be associated with poor performance, collapse, and sudden death. These events have catastrophic consequences for all participants in equine sport. By being able to prioritize horses for evaluation and improve our understanding of normal electrocardiogram findings, this study aims to improve identification of horses at risk of arrythmias, benefiting the safety of both horses and humans.

This research is under review at *Eq Vet J*.

Effects of Lasix (furosemide) on the hormone system responsible for blood pressure regulation (Grant #21-07)

Investigators: Jessica Morgan, DVM, PhD, DACVSMR, Marisa Ames, DVM,

DACVIM, Mallory Lehman, DVM

Furosemide, a commonly used diuretic, activates the renin-angiotensin-aldosterone system (RAAS) in non-equine species, but little is known about RAAS activation in horses. The objective of this study was to measure circulating angiotensin peptide (AP) concentrations in horses at baseline and in response to the administration of furosemide to improve our understanding of RAAS activation. A secondary aim of this study was to correlate the use of routine sample handling (the RAS-Fingerprint® analysis using equilibrium dialysis) to immediate protease-inhibited sample handling. Equilibrium dialysis results were analogous to immediate protease inhibition, supporting the use of this practical approach to RAAS analysis in the horse. Baseline levels of circulating APs were low in healthy horses compared to the levels described for other species. Only Angiotensin II was consistently detectable in healthy unstimulated horses. Furosemide produced an increase in hormones associated with both the classical and alternative RAAS pathways. Specifically, there was an increase in Angiotesin I, Angiotensin II, Angiotensin IV, Angiotensin 1-5 and aldosterone in furosemide-treated horses 4 hours after administration. This comprehensive RAAS data raises new questions about the evolutionary advantages of decreased RAAS activation in the horse and provides critical fundamental knowledge to study RAAS activation in cardiovascular and kidney disease.

How does this research benefit horses? Horses have remarkably low circulating RAAS activity compared to other species. Furosemide, a common diuretic used in horses, activates RAAS in the horse at doses commonly used in clinical practice. This information provides critical baseline information to direct the future study of this hormone system as a biomarker for disease and a therapeutic pathway in disease treatment.

SURGERY/ANESTHESIOLOGY

Morphine concentrations in the carpal joints after intravenous regional limb perfusion (Grant #21-V)

Investigators: Isabelle Kilcoyne, MVB, DACVS-LA, Jorge Nieto, MVZ, PhD DACVS, DACVSMR, Bridget F. Nottle BVSc, DACVS-LA, Harriet Flynn MVB, DACVAA, Heather K. Knych, DVM, PhD, DACVCP

Intravenous regional limb perfusion (IVRLP) is a commonly used technique to deliver high concentrations of antibiotics to the distal limb when treating wounds, septic arthritis, or osteomyelitis. These conditions can be very painful and co-administration of morphine, which is an opioid analgesic, may provide substantial pain relief for these conditions with fewer side effects than have been associated with systemic administration. The main objective of this study was to determine morphine concentrations in the carpal joint following IVRLP with morphine alone or in combination with amikacin (a commonly administered antibiotic). This was a randomized crossover study. Six horses underwent IVRLP with 0.1mg/kg morphine sulfate diluted to 60 mLs using 0.9% NaCl (M group) or combined with 2g amikacin and 0.9% NaCl (MA group) with a 2-week washout period between treatments. Synovial fluid was collected from the radiocarpal joint (RCJ) at different time points after IVRLP. The tourniquet was removed after the 30-minute sample was collected. Synovial concentrations of morphine and major metabolites were measured using liquid chromatography–tandem mass spectrometry. Amikacin concentrations were quantified by a fluorescence polarization immunoassay. Measurable concentrations of morphine were apparent in the RCJ of all horses. Peak concentrations of morphine in the M group were 4753.1 (2115.7-14,934.5) ng/mL and 4477 (3434.3-7363) ng/mL in the MA group (p=0.5). Median peak concentrations of synovial amikacin were 322.6 (157.5-1371.6 g/mL). IVRLP using morphine is a feasible technique and synovial morphine concentrations were measurable following IVRLP and were not affected when used concurrently with amikacin. Administration of morphine via IVRLP may be beneficial as an analgesic technique for orthopedic conditions of the distal limb while limiting potential serious systemic side effects.

How does this research benefit horses? Administration of opioids via IVRLP has potential benefits as an analgesic and anti-inflammatory agent in horses with painful, traumatic conditions of the distal limb, while potentially limiting the negative gastrointestinal effects associated with systemic administration. Techniques to improve weight bearing in horses with severe orthopedic injuries is paramount to reduce the incidence of complications such as support-limb laminitis.

This research was reported in *Eq Vet J* 2024 June 17 (online ahead of print)

MEDICINE & INFECTIOUS DISEASE

To investigate if vaccines are less effective in horses that receive immuno-suppressive drugs such as dexamethasone

Investigators: *Resident:* Nicole Kreutzfeldt, DVM, *Co-investigators:* Thomas M Chambers, PhD, Stephanie Reedy, Kennedy Spahn, *Mentor:* Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Corticosteroids such as dexamethasone are commonly used to treat horses; however, the effects of these immuno-suppressive medications on the immune response to vaccination is not well understood. In this study, horses that received one or several doses of dexamethasone at the time of vaccination did not have lower antibody levels at 30 days after vaccination against equine influenza compared to horses that did not receive any dexamethasone. However, horses that received multiple doses of dexamethasone (i.e. 3 intravenous doses at 24-hour intervals) at the time of vaccination had lower antibody levels at 30 days after vaccination against equine herpes virus 1 compared to horses that did not receive any dexamethasone. Multiple doses of dexamethasone at the time of vaccination may dampen the immune response in horses depending on the type of vaccine used. It remains unclear if the lower levels of antibodies are still protective against disease.

How does this research benefit horses? Veterinarians should be cautious when using multiple doses of dexamethasone to treat horses around the time of vaccination to prevent the risk of a potential vaccine failure and thereby increased risk of spread of infectious diseases in the horse population.

This research was reported in *J Vet Intern Med* 2024;38(1):424-430.

REPRODUCTION

Effect of euthanasia solution on oocyte's developmental competence and fertilization

Investigators: *Resident:* Soledad Martin-Pelaez, DVM, DACT, *Co-investigator:* Margo Verstraete, DVM, *Mentor:* Pouya Dini, DVM, PhD, PhD, DACT, DECAR

The collection of oocytes from mares' ovaries before or immediately after euthanasia is the last resource for producing offspring from these animals. However, it was unclear how euthanasia solution affected the production of embryos. In this study, we tested the effect of pentobarbital, a euthanasia agent commonly used in horses, on the developmental competence of oocytes. We evaluated the presence of pentobarbital in follicular fluid after euthanasia, and observed that this drug reaches the oocyte's environment almost immediately. Then, we used a bovine in vitro embryo production model to evaluate the potential toxicity of this drug on embryo development. We found a lower maturation rate of oocytes, but with an equal embryo development capacity. Lastly, in a follow-up study on equine oocytes, we observed the same trends as in the bovine model. The results of our study shed light on an unknown area of clinical practice: do we need to remove ovaries before or after euthanasia if the goal is in vitro embryo production? According to our results, removing ovaries under anesthesia prior to euthanasia is the most desirable protocol, as we could obtain a higher total number of embryos. On the other hand, due to logistical considerations, this is not always possible in the day-to-day equine practice, so we as also demonstrated that production of embryos from oocytes that have been exposed to pentobarbital is possible.

How does this research benefit horses? The production of offspring from critically ill and injured mares that must undergo euthanasia is a key resource to maintain and rescue valuable genetics. It is also an invaluable resource for owners that must make the hard decision to euthanize their mares and would like to have their progeny. Improving the techniques for post-mortem gamete retrieval and in vitro embryo production is key to ensuring this process is successful. The reproductive toxicity of euthanasia agents is an enigma that needs to be solved to increase the success rates. Here, we demonstrated the rapid presence of pentobarbital in the follicle after the administration of the drug and showed its effect on embryo production. Our research will aid owners and veterinarians in making informed decisions regarding euthanasia, while also encouraging the industry to explore post-mortem in vitro embryo production. Our study showed that, although it is less beneficial to remove the ovaries after euthanasia, the oocytes are still capable of producing embryos.

This research was reported in *Theriogenol* 2023;205:1-8.

SURGERY

Comparison of durations of perfusate injection for delivery of antibiotics to horses undergoing regional perfusion

Investigators: *Resident:* Laurel Saldinger, DVM, *Mentor:* Isabelle Kilcoyne, MVB, DACVS-LA

Joint infections in horses are a very serious medical condition that may lead to lameness, loss of performance, and even euthanasia. To aid in treatment of equine distal limb joint infection, regional administration of antimicrobials (intravenous regional limb perfusion) is commonly performed. Antimicrobials are infused into the leg via injection into the venous circulation distal to a tourniquet. In this study, two possible durations of time for perfusate instillation were evaluated to see if there was a change in joint or systemic concentrations.

The results of this study found that faster administration of perfusate (given over 1 minute) did not result in a significant change in joint concentration of antibiotic when compared to slower administration (5 minutes). However, faster administration did increase the systemic concentration of antibiotic during the perfusion. This suggests that faster instillation of perfusate results in leakage from the tourniquet and supports the practice of slower perfusate instillation time in practice.

How does this research benefit horses? Results from this research will help to provide equine clinicians with the best technique for achieving maximum concentration in the radiocarpal joint following intravenous regional limb perfusion with minimal systemic leakage. This will help to provide the best care for horses with orthopedic infections.

PARTNERSHIPS LEAD TO INNOVATIONS IN VETERINARY CARE

One of the many strengths of the UC Davis School of Veterinary Medicine is the guiding principle of collaboration in a multi-disciplinary approach to solve complex problems. These partnerships combine to investigate disease, improve techniques, identify treatments and advance knowledge.

Claire Giannini Hoffman Equine Athletic Performance Laboratory (EAPL) – This state-of-the-art, climate-controlled facility includes two high-speed Mustang treadmills, a video motion analysis system, and laboratory equipment and support necessary to perform in-depth investigations of respiratory, cardiac, musculoskeletal, and metabolic causes of poor performance and exercise intolerance. The EAPL is home to an integrated multidisciplinary clinical and research equine sports medicine program developed by emeritus faculty Dr. Jim Jones, an internationally-renowned equine exercise physiologist, and supported by faculty from the veterinary hospital's Equine Surgery and Lameness, Diagnostic Imaging, and Medicine Services.

J.D. Wheat Veterinary Orthopedic Research Laboratory – This laboratory provides an environment for conducting multidisciplinary studies pertaining to musculoskeletal disorders of animals and humans. Researchers associated with the laboratory work to understand the physiologic process of injury and musculoskeletal disease in performance, companion and production animals, as well as in humans.

William R. Pritchard Veterinary Medical Teaching Hospital Large Animal Clinic

Kenneth L. Maddy Equine Analytical Chemistry Laboratory – This laboratory provides a drug testing program with the highest quality standards, employing the most innovative methodology and newest analytical technology, in order to ensure the integrity of horse racing. The laboratory's mission includes expanding and disseminating new information regarding therapeutic medications in order to improve the welfare of California performance horses. It is part of the national Horseracing Integrity and Welfare Unit (HIWU), playing a vital role in the Horseracing Integrity and Safety Act's (HISA) drug control program.

Veterinary Center for Clinical Trials – The Veterinary Center for Clinical Trials (VCCT) is advancing medical care for horses by developing and investigating alternative diagnostic approaches for a variety of diseases. The VCCT is frequently enrolling equine patients for a variety of studies, ranging from cardiology to orthopedics.

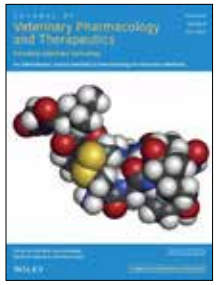
Veterinary Genetics Laboratory – The Veterinary Genetics Laboratory (VGL) provides animal parentage verification, identification, forensics services, genetic diagnostics and genetic disease research. The laboratory is internationally recognized as a pioneer and expert in DNA-based animal testing. The VGL also offers an extensive animal forensic services program, diagnostic tests for genetic diseases, and support for genetic research in domestic species, primates and wildlife. The laboratory is accredited by the ANSI National Accreditation Board.

Veterinary Institute for Regenerative Cures – The Institute has established laboratory techniques and animal models that are used to study regenerative therapies for veterinary and human medicine. It has characterized equine stem cells isolated from different tissues with a focus on adult-derived mesenchymal stem cells. The Institute has a foundation in collaborative, interdisciplinary "disease teams" that include basic research faculty and clinical faculty that focus on "bench to bedside" translation of stem cell therapies

William R. Pritchard Veterinary Medical Teaching Hospital – The William R. Pritchard Veterinary Medical Teaching Hospital provides innovative equine care by board-certified experts in equine medicine and surgery at the most advanced and comprehensive veterinary hospital in the world. The UC Davis veterinary hospital is accredited by the American Animal Hospital Association (AAHA), a distinction earned by less than 15% of animal hospitals in the United States and Canada.

PUBLICATIONS

Drug Therapies



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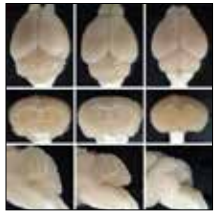

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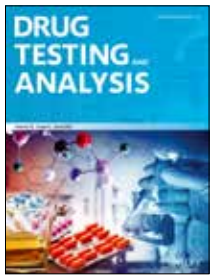

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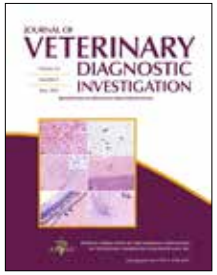

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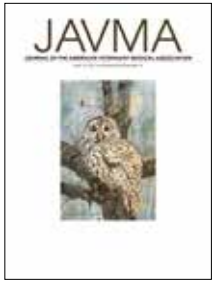

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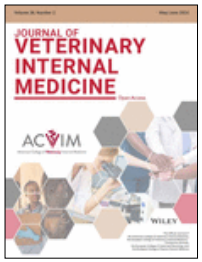

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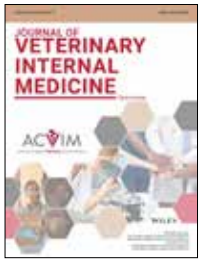

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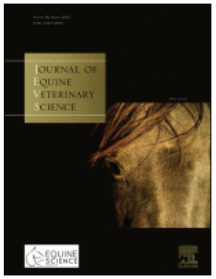

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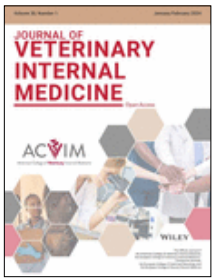

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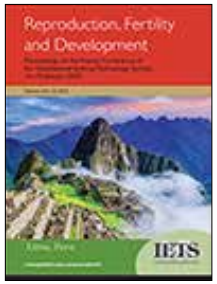

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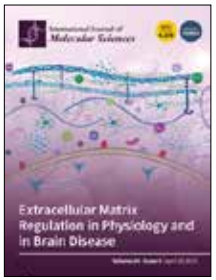

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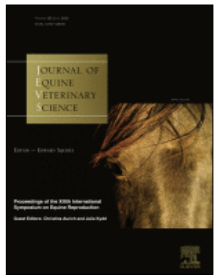

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NEWLY FUNDED RESEARCH STUDIES

DRUG THERAPIES

- Characterization of a novel treatment for gastric ulcers in horses
- Distribution of alprazolam into the milk of lactating mares and subsequent absorption by nursing foals
- Effect of ertugliflozin, a sodium-glucose cotransporter-2 inhibitor, on dexamethasone-induced insulin dysregulation in healthy horses
- Optimization of transdermal buprenorphine administration to horses
- Pharmacokinetics of oral marbofloxacin in adult horses
- Pharmacokinetics and safety of oral fluralaner at 10 and 25 mg/kg in the horse
- Thermal nociceptive effects of oral morphine in horses

GENETICS

- Characterizing genetic loci associated with insidious uveitis in LP-spotted horse breeds
- Investigation of genetic susceptibility for chronic progressive lymphedema in draft horses
- Investigating the connection of variants in pigmentation genes and insulin dysregulation in the horse
- Long-range sequencing for equine neuroaxonal dystrophy (eNAD)
- Using spatial transcriptomics to diagnose causes of non-infectious neurologic disease in the horse
- Validating the genetic cause for equine juvenile spinocerebellar ataxia

MEDICINE & INFECTIOUS DISEASE

- Defining metabolic status in mules creating reference ranges related to metabolic disease
- Determining the association between EHV-4 viral shedding and environmental contamination
- Development of a high fidelity model for puncture of atlanto-occipital site
- Investigation of the detection frequency of respiratory pathogens in healthy sport horses and their environment during the Traverse City horse show period
- Investigating the use of an air sampler for the detection of equine airborne respiratory pathogens
- Quantitative microbial evaluation of Armatrex antimicrobial solution

ORTHOPEDICS & LAMENESS

- Mitigating the adverse effects of Diclofenac on tendon cells with Vitamin C
- Promoting tendon formation with dipeptide prolyl-hydroxyproline

REPRODUCTION

- Do endometrial organoids resemble in vivo conditions? Effects of steroids on equine endometrial organoids
- Embryo-maternal communication in mares during pre-implantation (fixation) period
- Exploring bacterial metabolite and gene expression during equine placentitis
- The influence of the reproductive cycle stage on equine endometrial organoid formation and function
- X-chromosome inactivation in equine placenta and fetal tissues

SPORTS MEDICINE

- Evaluation of the feasibility of a cardiorespiratory screening protocol in the Thoroughbred Racehorse

CENTER FOR EQUINE HEALTH RESEARCHERS

Verena Affolter, DVM, Ph.D., DECVP

Dr. Verena Affolter received her veterinary degree from the University of Berne in Berne, Switzerland, where she also completed training in anatomic pathology. She completed a residency at Cornell University in Ithaca, NY and her PhD at the University of California Davis. Dr. Affolter is a diplomate of the European College of Veterinary Pathology and is a professor in the UC Davis School of Veterinary Medicine's Department of Pathology, Microbiology and Immunology. She serves as the Chief of Service in Anatomic Pathology, with an emphasis on dermatopathology and immunopathology. She is a past president of the International Society of Veterinary Dermatopathology. Her research interests include histiocytic and lymphocytic proliferative diseases, vasculitis, immune-mediated skin diseases, and chromic progressive lymphedema in horses.

Monica Aleman, MVZ, Ph.D., DACVIM (LAIM, Neurology)

Dr. Monica Aleman obtained her veterinary degree at the University UNAM-Mexico. She completed residencies in large animal internal medicine (equine emphasis) and neurology and neurosurgery at UC Davis and achieved board certification for both specialties by the American College of Veterinary Internal Medicine. She completed a PhD in comparative pathology of neuromuscular diseases at UC Davis. Her research and clinical interest has focused in neurology, neuromuscular and muscle disorders in all species, with an equine emphasis. Dr. Aleman is a faculty member in the equine internal medicine and neurology services and Co-Director of the Neuromuscular Disease Laboratory at UC Davis. She is one of the founding members of the Equine and Comparative Neurology Research Group and is affiliated with the Clinical Neurophysiology Laboratory at UC Davis.

Rebecca Bellone, Ph.D.

Dr. Rebecca Bellone earned her Ph.D. in Equine Genetics from the University of Kentucky in 2001. Subsequently, she has led an equine genetics research program involving both graduate and undergraduate students investigating the genetics of pigmentation and ocular disorders and the connection between the two. Her research team has collaboratively discovered causative mutations for both congenital stationary night blindness and ocular squamous cell carcinoma in horses. She is currently an Associate Adjunct Professor in the Department of Population Health and Reproduction and is the Director of the Veterinary Genetics Laboratory, a unit of the UC Davis School of Veterinary Medicine with an international reputation as experts in veterinary genetic testing.

Emily Berryhill, DVM, DACVIM

Dr. Emily Berryhill obtained her veterinary degree from the University of California, Davis, School of Veterinary Medicine in 2010. She completed the Large Animal Internal Medicine Residency at the University of California, Davis, School of Veterinary Medicine in 2016 and obtained Diplomate of the American College of Veterinary Internal Medicine status in 2016. She is an assistant professor in the Department of Medicine & Epidemiology and a faculty clinician in the Equine Internal Medicine Service. Her research focus is on equine physiology, endocrinology, and oncology, with a specialty focus on equine internal medicine. Additionally, she has performed pharmacologic studies evaluating new medications in horses.

Robert Brosnan, DVM, Ph.D., DACVAA

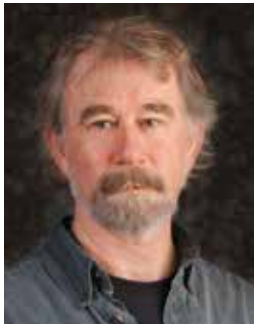
Dr. Robert Brosnan earned his veterinary degree from the UC Davis School of Veterinary Medicine in 1999, and a Ph.D. in Physiology from UC Davis in 2002. He is a diplomate of the American College of Veterinary Anesthesia and Analgesia. Dr. Brosnan has developed technology that has identified agents in several novel classes that could lead to better, safer and more cost effective general anesthetics for use in operating rooms and surgical centers. His research focuses on cardiovascular and respiratory effects of anesthetics and on the mechanisms of anesthetic action. Dr. Brosnan is currently a professor in the Department of Surgical and Radiological Sciences.

Jennifer Cassano, DVM, Ph.D.

Dr. Jennifer Cassano joined the Equine Field Service as an assistant professor in 2019. Dr. Cassano received her DVM (2013) and PhD (Comparative Biomedical Sciences, 2016) from Cornell University. Upon completion of graduate school, she completed a combined academic/private practice one-year rotating internship (2017) at the Cummings School of Veterinary Medicine, Tufts University/ Massachusetts Equine Clinic. She then worked as an associate veterinarian at EquidDoc Veterinary Services in Massachusetts. Her research interests and expertise are in the general area of stem cell biology and therapeutic actions of mesenchymal stem cells (MSCs), particularly in alterations in gene expression profiles of MSCs during exposure to inflammatory environments, and in the use of licensing agents to create more uniform MSCs exhibiting therapeutic traits such as chondroprotective activity.

Alessia Cenani, DrMedVet, MS, DACVAA

Dr. Alessai Cenani is an assistant professor in the Department of Surgical & Radiological Sciences. She received her veterinary degree from the University of Perugia, Perugia, Italy in 2009 and a Master's degree from the University of Liege, Liege, Belgium in 2012. Dr. Cenani came to UC Davis in 2016 for an anesthesia residency and subsequently became a diplomate of the American College of Veterinary Anesthesia and Analgesia. Her research focus is on pain management and recognition, as well as mechanisms of action of anesthetic and analgesic drugs, both in vitro and in vivo, with particular emphasis on assessment of drug efficacy in veterinary species.



Alan Conley, BVSc, MS, Ph.D., FRCVS, DACT

Dr. Alan Conley is a Professor Emeritus in the Department of Population Health & Reproduction, Director of the Clinical Endocrinology Laboratory, and holds the John P. Hughes Endowed Chair in Equine Reproduction. His veterinary degree was awarded by the University of Melbourne and he saw dairy practice and mixed practice in Australia and Scotland before completing a residency in theriogenology, and then Masters and PhD degrees at Iowa State University. He was an NIH Fellow at UT Southwestern Medical Center in Dallas, a Research Scientist with the USDA in Nebraska and on faculty at North Dakota State University before coming to UC Davis. He earned a Diploma of Fellowship from the Royal College of Veterinary Surgeons (FRCVS) in recognition of his contributions to comparative reproductive physiology. Much of this work has related to sex steroid synthesis, but in recent years with a particular focus on equine reproductive endocrinology and developing new diagnostic endocrine assays.

Julie Dechant, DVM, MS, DACVS, DAVECC

Dr. Julie Dechant received her DVM from the University of Saskatchewan in 1996 and completed an MS and surgical residency in 2000 at Colorado State University. After faculty appointments at Saskatchewan and Oklahoma State University, Dr. Dechant joined the UC Davis School of Veterinary Medicine faculty in 2004 and is currently a professor in the Department of Surgical and Radiological Sciences and chief of the equine emergency surgery and critical care service. Dr. Dechant is a diplomate of the American College of Veterinary Surgeons and the American College of Veterinary Emergency and Critical Care. In 2014, she was elected a Fellow in the Teaching Academy of the Consortium of West Region Colleges of Veterinary Medicine.

Pouya Dini, DVM, Ph.D., DECAR, DACT

Dr. Pouya Dini is an associate professor in the Department of Population Health and Reproduction. He completed his DVM at Karaj Azad University, Tehran, Iran in 2009 and a PhD from Azad University, Iran and Gent University, Belgium, in 2013. He completed a second PhD from Gent University, Belgium and the Gluck Equine Research Center in the U.S. in 2020. Dr. Dini is a diplomate of the European College of Animal Reproduction and the American College of Theriogenologists. His specialty focus is on the equine placenta and biotechnology of reproduction.

Ghislane Dujovne, DVM, MS, DACT

Dr. Ghislaine Dujovne obtained her DVM from the University of Chile, College of Veterinary Sciences in 2004, followed by her Diploma in Animal Reproduction with an equine emphasis. She worked in private general practice and as a reproductive consultant to numerous Thoroughbred breeding farms before beginning a residency in equine reproduction at Auburn University in 2008. Dr. Dujovne completed her residency and Master of Science degree in 2011, and remained at Auburn gaining experience as a clinical reproduction instructor. She is a diplomate of the American College of Theriogenologists. She joined the UC Davis School of Veterinary Medicine as an associate staff veterinarian and clinical professor in equine reproduction in 2012 and is currently an associate professor in the Department of Population Health and Reproduction and chief of the equine reproduction service.

Carrie Finno, DVM, Ph.D., DACVIM (LAIM)

Dr. Carrie Finno is an equine internist who received her DVM from the University of Minnesota. She then went on to complete a 3-year residency in large animal internal medicine at UC Davis, culminating in board certification in the American College of Veterinary Internal Medicine. Dr. Finno elected to pursue a career in equine genetic research, with a strong focus on neuromuscular disease, and obtained her PhD in 2012 from UC Davis. Dr. Finno's research is focused on equine genetic diseases, including equine neuroaxonal dystrophy/equine degenerative myeloencephalopathy (eNAD/EDM). In conjunction with the equine studies, she is researching the interaction of vitamin E and neural development, using a well-established mouse model. Dr. Finno was appointed as the director of the UC Davis Center for Equine Health in 2017 and is a professor in the Department of Population Health and Reproduction.

Larry Galuppo, DVM, DACVS-LA

Dr. Larry Galuppo is a Professor Emeritus in the Department of Surgical and Radiological Sciences. He graduated from the UC Davis School of Veterinary Medicine in 1990 and completed an internship at Rood and Riddle Equine Hospital in 1991. He completed an equine surgery residency at UC Davis from 1991 to 1994, and he has been on the faculty at UC Davis since 1996. His area of clinical expertise is in equine orthopedic surgery, including tendon, ligament and joint disorders, with a special interest in traumatology and fracture repair. His research emphasis is on the biomechanics of fracture generation, implant design and fracture repair, with a recent focus in management of musculoskeletal injuries using regenerative medicine therapies in sport horses.

Scott Katzman, DVM, DACVS-LA

Dr. Scott Katzman received his DVM from the University of Minnesota, College of Veterinary Medicine. Following four years in private practice, he returned to academia to complete a three-year residency in equine surgery at the UC Davis School of Veterinary Medicine. He is a board certified diplomate of the American College of Veterinary Surgeons. Following completion of his surgical training, Dr. Katzman spent the following two years as the staff surgeon at an equine referral clinic in Minnesota, as well as working at a variety of equine referral practices across the country before joining the UC Davis faculty. Dr. Katzman has a special interest in musculoskeletal injury in racehorses and upper respiratory surgery. He is currently an associate professor in the Department of Surgical and Radiological Sciences and chief of the equine surgery and lameness service.

Stefan Keller, DVM, Dr. Med. Vet., Ph.D., DECVP

Dr. Stefan Keller is an associate professor in the Department of Pathology, Microbiology, and Immunology. He earned his DVM from the University of Berlin, Germany in 2003, as well as his Dr. Med Vet. From the University of Zurich in 2007, Switzerland. He completed his PhD from UC Davis in 2015. Dr. Keller is a diplomate of the European College of Veterinary Pathologists. His research focus is on lymphoproliferative diseases and adaptive immunity.

Isabelle Kilcoyne, MVB, DACVS

Dr. Isabelle Kilcoyne earned her veterinary degree from the University of Dublin (Ireland) in 2008, after which she spent a year as an equine surgical intern at their University Veterinary Hospital. She then joined the UC Davis School of Veterinary Medicine, first as a team member with the Equine Field Service for two years, and then completed a three-year residency in equine surgery. Dr. Kilcoyne is an associate professor in the Equine Surgical Emergency and Critical Care Service. She is a board certified diplomate in the American College of Veterinary Surgeons. Her main clinical and research interests are in emergency surgery and medicine, particularly gastrointestinal surgery.

Heather Knych, DVM, Ph.D., DACVCP

Dr. Heather Knych is a professor of Clinical Veterinary Pharmacology. She earned her veterinary degree at the UC Davis School of Veterinary Medicine, followed by her PhD in pharmacology. She is a diplomate of the American College of Veterinary Clinical Pharmacology. Dr. Knych's research focuses on equine drug metabolism and pharmacokinetic/pharmacodynamics (PK/PD) relationships of drugs in performance horses. Additionally, Dr. Knych provides guidance to researchers at UC Davis and other universities as well as to drug companies on PK/PD study design. She assists with drug concentration determination and pharmacokinetic analysis in various biological matrices.

K. Gary Magdesian, DVM, DACVIM (LAIM), DACVECC, DACVCP

Dr. Gary Magdesian received his DVM from the UC Davis School of Veterinary Medicine and completed an internship in large animal medicine and surgery at the College of Veterinary Medicine at Texas A&M University. He then completed residencies in equine internal medicine, equine emergency medicine/critical care and clinical pharmacology at the School Veterinary Medicine, UC Davis. Dr. Magdesian is board certified in internal medicine, emergency/critical care and pharmacology. Currently, Dr. Magdesian is a professor in the Department of Medicine and Epidemiology and holds the Roberta and Carla Henry Endowed Chair in Emergency Medicine and Critical Care.

Beatriz Martínez López, DVM, MPVM, Ph.D.

Dr. Beatriz Martínez López received her veterinary degree from Complutense University, Madrid, Spain, in 2004 and her MPVM from the University of California, Davis in 2007. She earned a doctorate degree from Complutense University, Madrid, Spain in 2009. Dr. Martínez López is an associate professor in the Department of Medicine and Epidemiology and holds a faculty appointment with the Agricultural Experiment Station. She is also the Director of the UC Davis Center for Animal Disease Modeling and Surveillance (CADMS). Her research is focused on the development and application of epidemiological tools for supporting more cost-effective and risk-based surveillance and control strategies. She has primarily been working on epidemiological modeling and risk assessment for the evaluation of the potential introduction and/or spread of diseases affecting domestic and/or wild animal populations, many of which are considered to be emerging or re-emerging due to globalization, changes in climate and land use.

Stuart Meyers, DVM, Ph.D., DACT

Dr. Stuart Meyers, a Professor Emeritus in the Department of Anatomy, Physiology, and Cell Biology, earned his veterinary degree from the University of Michigan in 1985 and his PhD in comparative pathology from UC Davis in 1995. He is a diplomate of the American College of Theriogenologists. Dr. Meyers' research focuses on membrane and cytosolic events associated with sperm cell function and developing methods by which sperm preservation and fertility can be advanced. The laboratory is examining the role of membrane lipid domains and their associated proteins relative to sperm capacitation, osmotic and oxidative stress, and cryopreservation. Studies are aimed at optimization of male genome preservation and understanding of mechanisms of male subfertility.

Michael Mienaltowski, DVM, Ph.D.

Dr. Michael Mienaltowski earned his DVM degree from Michigan State University in 2004, followed by a PhD at the University of Kentucky in 2008. He continued with post-doctoral training at the University of South Florida from 2008 through 2014, with a focus on molecular pharmacology and physiology, orthopedics and sports medicine. He joined the faculty of the UC Davis College of Agricultural and Environmental Sciences in 2014 and is currently an associate professor in the Department of Animal Science.

Jessica Morgan, DVM, Ph.D., DACVSMR

Dr. Jessica Morgan joined the Equine Field Service as an assistant professor in 2019 and currently serves as chief of service. Dr. Morgan received her PhD (2012) and DVM (2013) from UC Davis. She completed an internship at Peninsula Equine Medical Center in Menlo Park, California, and a three-year residency in equine sports medicine and rehabilitation at the University of Pennsylvania School of Veterinary Medicine, New Bolton Center. Dr. Morgan remained at New Bolton Center as a lecturer in equine exercise physiology and then as a lecturer in large animal ultrasound and cardiology. She is a diplomate of the American College of Veterinary Sports Medicine and Rehabilitation. Dr. Morgan's research interests and expertise are in basic and applied science related to equine performance, musculoskeletal disease, and lameness diagnosis, including early detection and treatment of performance limiting conditions of horses and characterization of the roles that matricellular proteins play in tissue degeneration and disease prediction.

Nicola Pusterla, DVM, Ph.D., DACVIM-Equine

Dr. Nicola Pusterla graduated from the School of Veterinary Medicine at the University of Zurich, Switzerland in 1991. Dr. Pusterla worked in the private and academic sector with a focus in large animal internal medicine and earned his PhD from the University of Zurich with an emphasis on vectorborne diseases. He joined UC Davis in 1998, where he currently has an appointment as a professor in Equine Internal Medicine in the Department of Medicine and Epidemiology. Dr. Pusterla is a diplomate of the American College of Veterinary Internal Medicine with an equine emphasis, and he has ongoing interest in all aspects of equine internal medicine and dentistry. Dr. Pusterla's research focuses on selected aspects of equine infectious diseases with an emphasis on epidemiology, clinical disease understanding, diagnostics, prevention, and treatment.

Jeroen Saeij, Ph.D.

Dr. Jeroen Saeij earned his master's and doctorate degrees from Wageningen University, Wageningen, The Netherlands. He completed a postdoctoral fellowship at Stanford University before becoming a professor at the Massachusetts Institute of Technology. He is a professor in the Department of Pathology, Microbiology & Immunology at UC Davis. Dr. Saeij's research focus is on the molecular basis of pathogenesis of Apicomplexan parasites in humans and livestock. He is interested in how the interactions between parasite and host can lead to disease with a special interest in the genetic basis for individual host differences in resistance and parasite differences in virulence.

Joao Soares, MV, MSc, DSc, DACVAA

Dr. Joao Soares joined the Anesthesia/Critical Patient Care Service as an associate professor in 2018. He received his DVM in 1999 and his MSc in 2002 from the Fluminense Federal University, Brazil and his doctorate in 2012 from the Rio de Janeiro Federal University. He completed his residency in 2012 in veterinary anesthesiology at UC Davis and continued as a staff veterinarian from 2012-2014. Dr. Soares was an assistant professor of anesthesiology from 2014-2018 at the Virginia-Maryland Regional College of Veterinary Medicine. His research focuses on monitoring respiratory function during anesthesia, including linear and nonlinear models of respiratory mechanics, volumetric capnography, and on protective ventilation during anesthesia including monitoring ventilator settings and effects on outcome.

Mathieu Spriet, DVM, MS, DACVR, DECVDI, DACVR-EDI

Dr. Mathieu Spriet graduated from the National Veterinary School of Lyon, France in 2002. He completed an equine internship and master's degree at the University of Montreal (Canada). He completed his residency in diagnostic imaging at the University of Pennsylvania in 2007. Dr. Spriet is currently a professor of Clinical Diagnostic Imaging at the UC Davis School of Veterinary Medicine. He is a diplomate of both the American College of Veterinary Radiology and the European College of Veterinary Diagnostic Imaging. He recently became a diplomate of the newly recognized ACVR sub-specialty for Equine Diagnostic Imaging (2019). His main research interest is on musculoskeletal imaging. He has pioneered the use of Positron Emission Tomography (PET) in horses, leading to the development of an equine specific PET scanner.

Susan Stover, DVM, Ph.D., DACVS-LA

Dr. Susan Stover is a Professor Emeritus in the Department of Surgical and Radiological Sciences. She received her veterinary degree from Washington State University, and subsequently completed an equine surgery internship and residency at UC Davis. She was in equine practice in Washington State before returning to UC Davis to teach clinical equine lameness and surgery to veterinary students and residents. She became board certified by the American College of Veterinary Surgeons while pursuing a PhD program focused on equine orthopedic research (dorsal metacarpal disease ('bucked shins') in Thoroughbred racehorses). Dr. Stover now devotes her time to equine orthopedic research and teaches musculoskeletal anatomy, biomechanics, and pathology to veterinary students. She was honored with the American Veterinary Medical Association Lifetime Excellence in Research Award in 2016.

Alain Théon, DVM, MS, Ph.D., DACVR

Dr. Alain Théon received his DVM from Ecole Nationale Vétérinaire d'Alfort, (Maisons-Alfort France). He completed a 3-year research doctorate program in Radiation Biology at University Paris-Est (Creteil, France) concurrently with a 2-year internship in Radiation Oncology at Tenon Hospital (University Medical Center, Paris, France). He moved to the United States to pursue a training program in veterinary radiation oncology and completed a 2-year limited-status residency in Therapeutic Radiology at the UC Davis School of Veterinary Medicine. Dr. Théon completed a MS degree in Comparative Pathology at UC Davis funded by the Center for Companion Animal Health and joined the UC Davis School of Veterinary Medicine faculty in 1990. Since then, he has dedicated his career to teaching and research that benefits dogs, cats and horses with cancer. He is a Professor Emeritus in the Department of Surgical and Radiological Sciences.

Katherine Watson, DVM, Ph.D., DACVP

Dr. Katherine Watson is an associate professor at the California Animal Health and Food Safety Laboratory and the Department of Pathology, Microbiology and Immunology. She earned her PhD in 2014 and DVM in 2016, both from UC Davis. She is a diplomate of the American College of Veterinary Pathologists. Her specialty focus is in calcium nanoparticles and targeted nanotherapeutics.

Bart Weimer, Ph.D.

Dr. Bart Weimer is department chair, professor, and agronomist in the Department of Population Health and Reproduction. He earned his PhD from Utah State University in 1990 and was a postdoctoral fellow at the University of Melbourne, Australia in 1993. His research program is focused on population genomics of bacteria and ecological selection that leads to host association, pathogenesis, and long-term persistence that lead to induced metabolic shifts. He is the director of the 100K Genome Project, dedicated to sequencing the genomes of 100,000 bacteria and viruses that cause serious foodborne illnesses in people around the world.

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***Silver Stirrup Society members**

The Silver Stirrup Society is a unique equine organization that provides the Center for Equine Health with financial support for programs and activities that cannot be funded by state resources. The Silver Stirrup Society also provides a forum for sharing new advances in equine research and veterinary care. Membership is open to associations, clubs and individuals who contribute $1,000 or more annually to the Center for Equine Health. Lifetime memberships are offered to donors of larger gifts and bequests of $25,000 or more.

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EQUINE TRIBUTE AND MEMORIAL FUND

The Equine Tribute and Memorial Fund provides a meaningful way to pay tribute to special horses and the people that love them. Participating veterinarians, horse owners, friends, and family can honor horses that have passed, support those that have lost beloved horses, celebrate the birth of new foals, commemorate performance accomplishments, and pay tribute to individuals and organizations. Donations to this fund support cutting-edge equine research and valuable advances in equine veterinary care.

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A DEDICATED DONOR'S LEGACY AND LOVE FOR HORSES ENDURES

The equine community lost a valuable member, and the Center for Equine Health said goodbye to a beloved friend and donor, with the passing of Kathy Cromwell. She was dedicated to horses throughout her life and established the Equine Enduring Legacy Fund at UC Davis to ensure that horses would benefit from advanced veterinary care well into the future.

Kathy's championship buckles are on display at CEH.

An avid equestrian, Kathy was always in the top for year-end awards and was often show champion in trail divisions. She loved competitions and had a long career in open shows, Quarter Horse, and Paint Horse breed shows. Among her show horses were Opie's Misty, Thirsty Hobby, A Sudden Option (Lilly), and R Fancy Colored Zippo (Sunny).

Kathy's desire to give something of lasting value to equine healthcare and to owners struggling to support their horses in the face of veterinary challenges inspired her to create the Equine Enduring Legacy Fund. She established the fund for cases at the UC Davis veterinary hospital, and her endowment ensures support for horses in need for years to come. Use of the funds requires demonstration of unique medical or surgical cases that warrant publication as case reports, or cases that provide valuable teaching opportunities for veterinary students or residents. Our trainees take these learning experiences into their careers locally and globally, amplifying Kathy's goal of access to advanced veterinary care for all horses.

"Kathy Cromwell's forward thinking provides UC Davis with opportunities to push the envelope and advance veterinary medicine," said Dr. Gary Magdesian, Chief of the Equine Internal Medicine Service. "The Legacy Fund allows us to provide owners with hope of a chance to save horses with serious illnesses. Clinicians, residents, and students learn a great deal in the process. We are eternally grateful for Kathy's generosity and ingenuity."

Through the years, the Equine Enduring Legacy Fund has benefitted cases from foals to older horses, ponies to Percherons, and provided unique training to countless veterinary students and residents.

"The impact that Kathy has made is profound and will continue to live on for years to come," said CEH director Carrie Finno. "Every year, we would meet with Kathy and review cases supported by the Legacy Fund. There was true joy apparent in her ability to help these horses and their owners."

Kathy's horses Lilly and Sunny are living out their lives as part of the CEH Teaching Herd. They are kind teachers in our program and wonderful reminders of the enduring impact of one special equestrian's love of horses.

Kathy's horse Sunny is now a member of the CEH Teaching Herd.

SAYING GOODBYE TO OUR BELOVED PERCHERON LIBERTY

With heavy hearts, we had to say goodbye to our beloved draft horse Liberty in 2024. A staple of our teaching and outreach programs, as well as a participant in the Pioneer 100 Horse Health Project, Liberty was an outstanding ambassador for the CEH mission. If you have been at our facility in recent years, there is a good chance that you had the opportunity to meet this remarkable horse.

When Liberty came to CEH, he had neuromuscular signs that were ultimately diagnosed as vitamin E deficient myopathy. This condition is irreversible, but we were able to manage it successfully through daily vitamin E supplementation. His story, including both the challenges and the triumphs, was relatable to everyone, from children to adults, non-equestrians to seasoned riders.

We had battled some hoof ailments with Liberty, in particular an array of recurrent and severe hoof abscesses. Unfortunately, a lameness due to a deep right hind hoof abscess resulted in suspensory ligament breakdown of his left hind leg while he tried to support his weight. These injuries are extremely painful and challenging to treat, and nearly impossible in a horse of his size, age (21), and with his neuromuscular condition. Despite everyone's best efforts to make him comfortable, he let us know that it was time.

Liberty was loved by many and a favorite of the CEH staff and students. From the smiles to the tears, we are grateful to have known this gentle giant and so appreciative of his contributions. Special thanks to our colleagues at the Large Animal Clinic and farrier Shane Westman for being part of Liberty's healthcare team over the years.

We value your partnership in our mission to improve the health and well-being of horses.

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