

2022 CENTER FOR EQUINE HEALTH RESEARCH REVIEW

New Discoveries in Equine Health



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December 2022

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On the cover:

A representation of some of the CEH teaching herd horses that are enrolled in the Pioneer 100 Horse Health Project (see story page 50). The CEH Teaching Herd provides valuable hands-on learning opportunities to veterinary students, residents, and undergraduate and graduate students. The Center for Equine Health Teaching Herd Fund supports daily and specialized care for these horses.

Director's Message

Welcome to the *2022 Research Review*, focused on the research accomplishments of UC Davis faculty, residents, students, and staff as supported by the Center for Equine Health (CEH).

From the COVID-19 pandemic to equine herpes virus 1 (EHV1) outbreaks, the past two years have presented unique challenges. Our researchers navigated campus closures, supply chain bottlenecks, and many other speedbumps to generate the data presented here. We are especially proud to share the resulting research findings that epitomize the passion and commitment that make UC Davis a leader in equine research.

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 have investigated novel approaches to pain management in horses, the genetic basis for a variety of conditions, detection and management of infectious diseases, imaging and surgical options for orthopedic injuries, advances in equine advanced reproductive technologies, and much more.

This review also highlights the outstanding 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, and analyzing and publishing their findings.

Much of this research would not have been possible without our wonderful teaching herd of horses and the dedicated staff and students that care for them. Despite the challenges of the last few years, our horses are happy, thriving, and playing vital roles in improving health for all horses. They are at the heart of everything that we do, and we are grateful for their unique contributions to equine veterinary medicine.

Our research is supported by the generosity of the many donors who continue to make the Center's research program a success. **Thank you** to each and every donor for your investment in CEH for the health and well-being of horses today, and for years to come.



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





CENTER FOR EQUINE HEALTH SCIENTIFIC ADVISORY BOARD (2020 - 2022)

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CENTER FOR EQUINE HEALTH AWARDS

2020 James M. Wilson Award – Kelly E. Knickelbein, VMD, ACVO

Dr. Kelly Knickelbein received the 2020 James M. Wilson Award in recognition of her contributions to equine research. She was chosen for her publication entitled, “A missense mutation in damage-specific DNA binding protein 2 is a genetic risk factor for ocular squamous cell carcinoma in Belgian horses,” published in the *Equine Veterinary Journal* (2019, 52(1): 34-40). She completed the work under the mentorship of Drs. Mary Lassaline and Rebecca Bellone.



Dr. Kelly Knickelbein (L) with Dr. Mary Lassaline (R).

This study sought to determine if a previously identified genetic variant in the *DNA binding protein 2 (DDB2)* gene that is associated with ocular squamous cell carcinoma (SCC) in the Haflinger breed is also associated with the disease in the closely related Belgian breed. The data revealed that Belgian horses with two copies of the *DDB2* variant are at four times greater risk of developing ocular SCC than horses with a single copy or no copies. Since not every case in the dataset had two copies of the *DDB2* variant, it is suspected that additional genetic factors or environmental influences may explain some cases of ocular SCC in Belgian horses.

A genetic test for ocular SCC is now available through the UC Davis Veterinary Genetics Laboratory to identify Haflingers and Belgian horses at increased risk of developing the disease. This allows owners of high-risk horses to implement best management practices to decrease cancer risk, and enables

James M. Wilson Award

The James M. Wilson Award is given each year to an outstanding equine research publication authored by a graduate student or resident in the UC Davis School of Veterinary Medicine. The Center for Equine Health Scientific Advisory Board judges 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.

early detection and treatment. Testing of Belgian and Haflinger horses used for breeding can inform decisions on mate selection in order to limit the production of high-risk horses.

2021 James M. Wilson Award – Sarah Shaffer, PhD

Dr. Sarah Shaffer received the 2021 James M. Wilson Award for her publication entitled, “Subchondral focal osteopenia associated with proximal sesamoid bone fracture in Thoroughbred racehorses,” published in the *Equine Veterinary Journal* (2020, 53(2): 294-305). Her research was conducted at the J.D. Wheat Veterinary Orthopedics Research Laboratory under the direction of Dr. Susan Stover.

The most common cause of fatal injury among California Thoroughbred racehorses is proximal sesamoid bone (PSB) fracture. The PSBs are a pair of bones in the suspensory apparatus that support the back of the fetlock joint. When they fracture, the fetlock loses support and the horse cannot bear weight on the limb.

Until recently, there was no way to identify horses at risk for PSB fracture. This study discovered, characterized, and described changes that precede PSB fracture and put horses at risk for catastrophic fracture. Shaffer examined PSBs from racehorses that died due to PSB fracture during racing or training using microcomputed tomography, high-detail x-rays, tissue stains and other techniques. A bone bruise was observed below the joint surface that was not present in unaffected horses. This lesion showed a region of bone loss and evidence of high levels of microdamage.

These typical stress fracture characteristics provide guidance to veterinarians for injury prevention (via screening) and treatment. With the concurrent introduction of positron emission tomography (PET) scanning of the PSBs, the changes discovered allow affected horses to be identified and rehabilitated for return to training and competition.



Dr. Sarah Shaffer and her horse Beau

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.



Dr. Balasuriya (center) with CEH Director Dr. Carrie Finno (L) and Professor Emeritus Dr. James MachLachlan (R).

Salick Lecture

The Center for Equine Health was pleased to host the 2022 Salick lecturer Dr. Udeni Balasuriya, who presented “New Insights into EAV Persistent Infection in the Stallion Reproductive Tract”. Dr. Balasuriya is Director and Professor of Virology at the Louisiana Animal Disease Diagnostic Laboratory at the Louisiana State University School of Veterinary Medicine. His professional and research experience encompasses infectious diseases of animals and humans, veterinary diagnostic medicine (anatomic pathology and diagnostic virology), and molecular virology.

INNOVATION FUNDS

Alamo Pintado Equine Health Foundation Fund – This fund was established in memory of Dr. 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 various medical conditions of the animals and the development of improved treatment regimens.

Bernard and Gloria Salick 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 (see sidebar previous page).

Dan Evans Memorial Endowment – The Dan Evans Memorial Endowment provides funding for UC Davis Veterinary Medical Teaching 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 the clinical trials program 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.

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 Medical Teaching 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 Veterinary Medical Teaching 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 – This fund was established by longtime Silver Stirrup Society members, Patricia and Paul Yeretzian. The 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 Medical Teaching Hospital to conduct equine respiratory disease and colic research.

Performance Horse Endowment – Medical problems of the mature show and event horse are the focus of the Performance Horse Endowment. This endowment also 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.

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

Implications of cytochrome P450 2D50 polymorphisms on drug clearance (Grant #18-05)

Investigator: Heather Knych, DVM, PhD, DACVCP

Considering the large degree of individual variability between horses, establishing an appropriate treatment regimen for a drug can provide a challenge to veterinarians. Variability in the activity of drug metabolizing enzymes attributable to genetic mutations is one documented reason for these differences in other species. The goal of this study was to begin to assess whether mutations in drug metabolizing enzyme genes can impact drug behavior in horses. Codeine was chosen as the test drug and was administered orally to 12 research horses and blood samples collected. Drug concentrations were measured and used to select times for collection of blood samples in a larger population of horses. Following administration of codeine to this larger group of horses, drug concentrations were measured in blood and the relative amount of metabolism of codeine determined. Based on the relative metabolism of codeine to metabolite, horses were categorized as low, normal and rapid metabolizers. A subset of horses was selected for whole genome sequencing and investigation of potential genetic mutations in drug metabolizing enzyme genes. Codeine was well tolerated following oral administration and was rapidly converted to five different metabolites. The range of codeine metabolism determined in this study identified a strong candidate gene for the metabolic enzyme, *CYP2D82* in the horse and warrants further investigation of the implications of this finding on the clinical effect of drugs that are metabolized by this enzyme in horses.

How does this research benefit horses? Data gathered in this study provides some insight into why differing responses are observed between horses when drugs that are metabolized by the *CYP2D* enzyme are administered. Information from this study could potentially be used to develop a simple test, similar to that available for humans, which may aid in the development of individualized therapeutic regimens (“personalized medicine”) for each horse under care.

This research was reported in *Veterinary Anaesthesia and Analgesia* 2020;47:694-704 and *BMC Veterinary Research* 2021;17(77).

Pharmacokinetics and physiologic effects of meperidine in horses (Grant #18-11)

Investigator: Heather Knych, DVM, PhD, DACVCP

Pain management is an important component of patient care. In horses, there are a limited number of analgesic drugs that have been fully characterized. The goal of the current study was to begin to investigate the opioid drug, meperidine, which is similar in its actions to morphine, as a potential analgesic in horses. Eight horses, on four different occasions, received a single intravenous administration of meperidine (0.5, 1 or 2 mg/kg) or saline. Blood samples were collected up to 96 hours following drug administration, drug concentrations measured, and pharmacokinetic parameters determined. Pre- and post-drug related behavior, locomotor activity, heart rate and gastrointestinal function were recorded. Response to noxious stimuli was evaluated by determining the response to application of heat. Meperidine was rapidly cleared following IV administration of all three doses; however, adverse effects including excitation, increases in heart rate and the development of hives were noted with higher doses. While meperidine did prevent horses from responding to the application of heat, the response was short-lived (up to 45 minutes). Results of this study do not support routine clinical use of meperidine at a dose of 1 mg/kg IV. Administration of a dose of 0.5 mg/kg decreased the response to the application of heat but the effect was short-lived, and the associated adverse effects suggest its use as a sole agent at this dose should be cautiously considered.

How does this research benefit horses? A limited number of analgesics have been variably characterized in horses. This study was designed to begin to assess the potential of the opioid meperidine as an additional option for pain relief in the horse.

This research was reported in *BMC Veterinary Research* 2020;16(368).



Characterization of a novel opioid analgesic in horses (Grant #19-04)

Investigator: Heather Knych, DVM, PhD, DACVCP

Morphine is a potent pain-relieving drug. However, reports of adverse effects at clinical doses limits its use in horses. In other species, pain-relieving and adverse effects have been attributed, at least partly, to two distinct metabolites of morphine (M3G and M6G). The goal of this study was to describe how the horse processes the presumed pain-relieving metabolite (M6G) and determine its effects following intravenous administration. Seven horses received a single intravenous administration of saline, 0.5 mg/kg morphine sulfate and 0.01 mg/kg M6G with a 2-week drug free period between doses. Blood samples were collected up to 96-hours for determination of drug concentrations. Drug related behavior and physiologic responses were recorded. Response to noxious stimuli was evaluated by determining response to the application of heat at several times post administration. M6G was cleared more rapidly than morphine. Morphine administration resulted in signs of excitation, whereas M6G appeared to cause sedative like effects. The response to a heat stimulus was significantly reduced until 4 hours post morphine administration and 1-hour post M6G administration. A more favorable safety profile compared to morphine, coupled with favorable effects on response to a noxious stimuli (heat), are encouraging for further study of the effects of higher doses of M6G in the horse.

How does this research benefit horses? Results of this study provide data to support further study of the morphine metabolite, M6G, as a pain medication for horses, devoid of the adverse effects associated with morphine administration.

This research was reported in *Veterinary Anaesthesia and Analgesia* 2022;49(6):634-644.

GENETICS

Validating a diagnostic test for equine neuroaxonal dystrophy (Grant #18-02)

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

During the first year of life, certain foals may develop an inherited neurologic disorder known as equine neuroaxonal dystrophy (eNAD). Until recently, the only way to definitively diagnose eNAD was on postmortem examination. Our previously funded studies from the Center for Equine Health allowed us to evaluate how vitamin E is metabolized in affected horses while investigating possible genetic regions associated with eNAD. Excitingly, we have recently discovered that eNAD-affected horses metabolize vitamin E, specifically α -tocopherol, at a faster rate than age-matched unaffected horses. The next step is to perform this test in a larger number of horses, thereby validating the test as a way to diagnose eNAD. We hypothesized that eNAD-affected horses metabolize vitamin E, specifically α -tocopherol, at a faster rate than unaffected horses. We discovered that, similar to ataxia with vitamin E deficiency in humans, eNAD-affected horses metabolize α -tocopherol, but not λ -tocopherol, at a faster rate than unaffected horses.

How does this research benefit horses? Abnormal α -tocopherol metabolism has been identified in ataxia with vitamin E deficiency in humans. Similar to that disease, horses with eNAD demonstrate a higher rate of metabolism of α -tocopherol than healthy horses. This further strengthens the link between eNAD and vitamin E deficiency and may provide an antemortem diagnostic assay.

This research was reported in the *Journal of Veterinary Internal Medicine* 2021;35(5): 2473-2485.

Discovering a genetic mutation for elevated gamma-glutamyltransferase (GGT) concentrations in Thoroughbred racehorses (Grant #18-9)

Investigators: Carrie J. Finno, DVM, PhD, DACVIM (LAIM), K. Gary Magdesian, DVM, DACVIM (LAIM), DACVECC, DACVCP, Joseph Dowd, DVM, PhD

Elevations in serum gamma-glutamyltransferase (GGT) activity (i.e. “high GGT syndrome”) have been reported in Thoroughbred racehorses and associated with poor racing performance. The reasons for these increases in GGT are not known. Our proposal aimed to investigate an underlying genetic cause for isolated elevations in serum GGT concentrations in Thoroughbred racehorses



using a combined approach of a genome-wide association study and whole-genome sequencing. We identified a region of suggestive genetic association on chromosome 5 for high GGT syndrome in Thoroughbred racehorses. Associated genetic markers in this region surround one candidate gene, cluster of differentiation 1a (*CD1A1*), a transmembrane gene related to the major histocompatibility complex. This candidate gene requires further evaluation in a larger cohort of high GGT horses.

How does this research benefit horses? Abnormally high serum gamma-glutamyltransferase (GGT) is observed in Thoroughbred racing horses, particularly among those with a poor racing performance. In this study, we identified a possible underlying genetic region of association for high GGT syndrome in racing Thoroughbreds.

This research was reported in the *Journal of Veterinary Internal Medicine* 2022;36(6):2203-2212.

Finding the genetic mutation for inherited epilepsy in Arabian foals (Grant #18-10)

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

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. In children with similar benign familial neonatal convulsions, genetic mutations have been identified in the potassium voltage-gated channel genes, *KCNQ2* and *KCNQ3*. In the horse, JIE is inherited and our previously funded studies from the Center for Equine Health allowed us to identify a genetic region of interest associated with JIE. We then used whole-genome sequencing to find possible underlying mutations in this region in two JIE-affected horses. The region identified did not contain any strong candidate genes. However, sequence commonalities were identified to a region with a strong candidate gene, *KCNQ1*. We hypothesized that, either due to errors in the reference genome or structural rearrangements in JIE-affected foals, the underlying mutation for JIE resides in *KCNQ1*. This genetic mutation may result in a different proportion of the two RNA products produced.

Long-range sequencing was performed using Nanopore technology in

one affected and one unaffected foal with the associated haplotypes on chromosome 1. These sequences were then assembled into contiguous regions (i.e. “contigs”) that surrounded the region of interest. The homozygous contig for the JIE-affected foal correlated with the contig for the unaffected foal, suggesting no large homozygous structural variations. Direct genotyping of four putative genetic markers in *KCNQ1* that were identified in the n=2 short-read whole-genome sequenced JIE foals were genotyped in a subset of affected (n=3) and unaffected (n=6) foals via Sanger Sequencing and no association was identified. Therefore, a structural rearrangement between chromosomes 1 and 12, in the region of *KCNQ1*, was excluded.

How does this research benefit horses? Epilepsy can result in loss of animals and a major financial burden due to elevated costs of antiepileptic treatment and hospitalization. Therefore, the identification of genetic variants will aid in strategic breeding and avoid the perpetuation of genetic mutations that affect the overall health and well-being of the Arabian breed.

This research was reported in *Genes* 2019;10(10): 1-4.

Genetic investigation of equine recurrent uveitis in the Knabstrupper breed (Grant #18-16)

Investigators: Rebecca Bellone, PhD, Lynne Sandmeyer, DVM, DVSc, DACVO, Nicole Kingsley, PhD

Equine recurrent uveitis (ERU) is the leading cause of blindness in horses. It has been documented in several breeds with the leopard complex spotting patterns (Appaloosa, Knabstrupper, Pony of the Americas). This investigation characterized prevalence, clinical features, and risk factors in the Knabstrupper breed. By evaluating horses in Denmark, Sweden, and the USA, it was determined that uveitis in the Knabstrupper is clinically very similar



to a subset of ERU, insidious uveitis, in the Appaloosa. Risk for this eye disease increased with age as did having two copies (homozygous) of the genetic variant that causes the leopard complex spotting patterns (LP). Therefore, genotyping for LP can assist with clinical and breeding decisions related to insidious uveitis in this breed. This analysis also determined that additional genetic loci likely contribute to disease risk in this breed and further genomic investigations are warranted.

How does this research benefit horses? Equine recurrent uveitis is a complex disorder with several different etiologies suspected, but little is known about the mechanisms underlying this blinding disease within and across equine breeds. From this research, we have a better understanding of the clinical signs of ERU, specifically in the Knabstrupper. Additionally, this research identified two significant risk factors (age and LP genotype). Based on the findings of this study, more frequent clinical evaluation are recommended for Knabstrupper horses between the ages of 11-20 years old with the LP/LP genotype to identify and manage early signs of disease.

This research was reported in the *Equine Veterinary Journal* 2022. Published ahead of print.

MEDICINE & INFECTIOUS DISEASE

Identification of vaccine candidates for the neurological disease equine protozoal myeloencephalitis (Grant #18-3)

Investigators: Tatiana Paredes-Santos, PhD, Jeroen P.J. Saeij, PhD

Equine protozoal myeloencephalitis (EPM) is a debilitating neurologic disease that is associated with infection with the protozoan parasite *Sarcocystis neurona*. There are currently no vaccines available against *S. neurona*. For rational vaccine design, a better understanding of the basic biology of *S. neurona* is needed. For example, it is currently unclear how *S. neurona* modulates the host cells it infects to eventually cause pathology. We hypothesize that a better understanding of *S. neurona*-host interactions will allow the future rational design of vaccines or better therapies. A vaccine against *S. neurona* would reduce the prevalence of



EPM. The goal of this study was to determine if the *Toxoplasma* secreted proteins that we know are important for *Toxoplasma* pathogenesis and that are conserved in *S. neurona* are also important for *S. neurona* pathogenesis.

We identified 13 *Toxoplasma* proteins that are conserved in *S. neurona* and are known to be involved in crucial *Toxoplasma*-host interactions. We used the latest genetic techniques to manipulate the genome of *S. neurona* in a way that would have allowed us to visualize the localization of these

conserved proteins. We also used genetic techniques to delete each of these genes individually in *S. neurona*. Unfortunately, we were unable to manipulate the genome of *S. neurona*. This shows that we will first need to optimize the technologies that we have previously established for *Toxoplasma* for *S. neurona*.

How does this research benefit horses? We want to determine which proteins *S. neurona* uses to acquire host nutrients or modulate the host cell. This will advance our understanding of *S. neurona*-host interactions. To date, no secreted proteins from *S. neurona* have been characterized. A better understanding of the basic biology of *S. neurona* will unveil new drug targets and vaccine candidates against EPM.

Prevention of viral respiratory infections in weanling foals by using an intra-nasal equine influenza vaccine (Grant #18-6)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, Jeanne Bowers, DVM, Samantha Barnum, MS, Virginia Hernandez, Rebeca Scalco

During stressful periods, such as weaning, foals can be more susceptible to viral respiratory infections, including equine herpes viruses. We hypothesized that an intra-nasal equine influenza vaccine, administered prior to weaning, would decrease the incidence of viral respiratory infections. Twenty healthy weaning foals received a single dose of FluAvert (equine influenza virus vaccine) 10 days prior to being weaned. An additional 20 healthy foals served as unvaccinated

controls. Nasal secretions were collected prior to the vaccine administration, on the day of weaning, and weekly thereafter for 6 weeks. The nasal secretions were tested by PCR for herpes viruses. Physical parameters were collected daily for the entire study period. Molecular and physical parameters were then compared between the groups. The use of FluAvert was associated with a better clinical outcome in vaccinates. However, the EIV vaccine was unable to influence selected hematological parameters and viral kinetics of herpesviruses. The clinical benefit observed in vaccinates may explain the overall perception that the use of the modified live EIV vaccine induces cross-protection against respiratory agents.

How does this research benefit horses? Due to the economic impact of contagious respiratory pathogens, it is relevant that horses be protected against respiratory viruses, especially during stressful times such as the weaning period. While today's vaccines offer a suboptimal protection against respiratory viruses, the use of local immunomodulators aiming at improving mucosal immunity could enhance anti-viral protection, therefore contributing to the overall health and wellbeing of horses.

This research was reported in the *Canadian Veterinary Journal* 2020;61:517-520.

Improving the molecular diagnostic field of *Clostridium perfringens* in foals with diarrhea

(Grant #18-15)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, K. Gary Magdesian, DVM, DACVIM, DACVECC, DACVCP, Nathan Slovis, DVM, DACVIM, CHT

Infections of *Clostridium perfringens* in foals are often severe and highly contagious. Thus, there is a need to improve the molecular diagnostic testing that is currently available in order to obtain rapid and accurate results. Feces from 50 healthy foals and 50 foals with diarrhea were collected for this study at two veterinary hospitals. The age of the study foals ranged from 1 week to 16 weeks. The samples were processed for nucleic acid extraction and tested for a



panel of five *C. perfringens* target genes (alpha, beta, *C. perfringens* enterotoxin, beta2 and netF). The samples were also tested by qPCR for established foal diarrhea pathogens including equine rotavirus, equine coronavirus, *C. difficile* toxin A and B, *Salmonella enterica*, *Lawsonia intracellularis*, *Neorickettsia risticii* and *Rhodococcus equi* in order to document mono- versus co-infection. The results showed that there was no difference in the frequency of *C. perfringens* type and virulence genes between healthy and sick foals. There was further no difference between the two groups in the frequency of shedding of *C. difficile*. *Salmonella enterica*, *N. risticii*, *L. intracellularis*, *R. equi*, and ECoV were not detected in any of the study foals. Equine rotavirus was the only enteric pathogen with a higher frequency of detection in foals with diarrhea ($P < 0.05$). The study results showed that the use of a *C. perfringens* panel, targeting various toxin genes, was unable to definitively determine the role of this enteric pathogen as a cause of diarrhea in foals.

Table summarizing results showing the frequency of *C. perfringens* type and virulence genes and Rotavirus detection between healthy and sick foals. The higher frequency of rotavirus detection in foals with diarrhea was the only significant difference ($P < 0.05$).

	<i>C. perfringens</i>					<i>C. difficile</i>	Rotavirus
	Alpha gene	Beta gene	Beta2 toxin gene	CPE gene	netF gene	Toxin A/B gene	
Healthy foals	36%	0%	18%	0%	18%	9%	0%
Foals with diarrhea	28%	0%	26%	4%	17%	11%	13%

How does this research benefit horses? Equine veterinarians recognize that diarrhea is extremely common in foals of all ages but the condition is often self-limiting and caused by infectious and non-infectious conditions. Sensitivity and specificity of diagnostic tests vary for different agents. This mainly depends

on the methodology but also relative prevalence of detection of the pathogens in healthy foals. Because of the severity and contagious nature of *C. perfringens* infections, reliable and timely qPCR assays may help manage foals with diarrhea. Unfortunately, the present study results showed that the detection of various virulence genes of *C. perfringens* was unable to differentiate between healthy foals and foals with diarrhea.

Study the role of *Toxoplasma gondii* as a cause of neurologic disease in horses (Grant #18-21)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, Patricia Conrad, DVM, PhD, Woutrina Smith, DVM, MPVM, PhD, Kaitlyn James, Eva Tamez-Trevino, Monica Aleman, MVZ, PhD, DACVIM (LAIM, Neurology), Pedro Bernardino, DVM

Equine protozoal myeloencephalitis (EPM) is caused by two recognized protozoal apicomplexan parasites, *Sarcocystis neurona* and *Neospora hughesi*. In other animal species, *Toxoplasma gondii* has been shown to be another protozoal parasite capable of causing encephalomyelitis. Banked serum and cerebrospinal fluid (CSF) samples from 210 horses with neurological deficits were analyzed for the detection of *T. gondii*, *S. neurona* and *N. hughesi* antibodies by immunofluorescence antibody test (IFAT). Based on a serum/CSF ratio ≤ 64 , horses were characterized either as *T. gondii*-suspect or as *S. neurona*/*N. hughesi*-suspect. Frequency of immunodiagnostic status was determined, as well as selected prevalence factors between *T. gondii*-suspect and *S. neurona*/*N. hughesi*-suspect EPM cases. Based on a serum/CSF ratio ≤ 64 , 22 and 43 horses fit the case definition of *T. gondii* and *S. neurona*/*N. hughesi* EPM-suspect, respectively. No statistically significant differences were found for age, sex, breed other than Warmblood, use, and clinical signs other than lameness between *T. gondii*- and *S. neurona*/*N. hughesi*-suspect EPM cases.

How does this research benefit horses? EPM is a common neurologic disease of equids, and many facets of its epidemiology are still considered missing



links. This study strives to illuminate the role of *Toxoplasma gondii* as another cause of neurologic disease in horses.

The results of this study showed that 10% of EPM-suspect horses had evidence of antibodies in the CSF to *Toxoplasma gondii*. Horses that were Warmbloods and lack of lameness were significantly associated with *T. gondii*-suspect horses when compared to horses infected with well-established apicomplexan protozoa (*S. neurona* and/or *N. hughesi*).

Using culture followed by PCR to determine the infectious nature of *Streptococcus equi* subspecies *equi*, agent of strangles (Grant #18-23)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, Barbara Byrne, DVM, PhD, DACVIM (Large Animal), DACVMBM, Samantha Barnum, MS

The diagnosis of strangles requires the detection of *S. equi* by microbiological culture, PCR, or both on samples from the upper respiratory tract. Recent studies have shown that PCR is more sensitive than bacterial culture, despite the fact that PCR is unable to determine viability of streptococcal organisms. The objective of the present study was to investigate a novel approach that combined a 24-hour selective culture step, followed by PCR, in order to characterize the viability of *S. equi* in biological samples. Nasal secretions collected from 42 horses with suspected strangles were tested by culture and by qPCR prior to and 24-hours following a culture step. Viable *S. equi* was determined based on the detection of *S. equi* via culture, the detection of mRNA transcripts for the *SeM* gene of *S. equi* by qPCR and/or an increase in absolute number of *SeM* target genes of *S. equi* between pre- and post-cultured samples. The overall agreement between culture alone and the three criteria to determine viability was 59%. The overall agreement for the detection of mRNA transcripts and increase in absolute target genes was 88% and 74%, respectively. The combination of mRNA transcripts and increase in absolute target genes was able to determine the viability status in all 42 samples.

How does this research benefit horses? The increasing application of qPCR for the detection of *S. equi* in practice settings has presented new dilemmas with regard to how test results are interpreted and used by equine practitioners since routine qPCR assays are unable to differentiate between viable streptococcal organisms from nonviable cells or from free nucleic acids in biological samples. The study results showed that, in the absence of a culture-positive result for *S. equi*, the determination of viability was achieved by using molecular strategies applied to samples undergoing a 24-hour culture step. Determining molecular viability of *S. equi* is essential in order to implement biosecurity protocols and reduce risk of transmission.

This research was reported in the *Journal of Equine Veterinary Science* 2021;97:103328.

Develop PCR assays able to differentiate between field and vaccine strains of *Streptococcus equi* subspecies *equi*, agent of strangles (Grant #19-14)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, Samantha Barnum, MS

The highly contagious, host-adapted bacterium, *Streptococcus equi* subspecies *equi* (*S. equi*), is the etiologic agent of equine strangles. *S. equi* primarily targets the lymphoid tissues of the upper respiratory tract of equids, which leads to acute swelling and abscess formation of mandibular and retropharyngeal lymph nodes. Killed or modified-live (ML) *S. equi* vaccines are commonly used in the prevention of strangles. However, the ML *S. equi* vaccine strain has retained some

virulence and has been associated with clinical disease post-vaccination. Because of the strong difference in contagiousness between vaccine (not contagious) and field (highly contagious) *S. equi* isolates, it is important to quickly differentiate between the two strain types. Field and vaccine strains associated infections can be differentiated using subtyping methods. These methods are costly and very time-consuming.

In order to further characterize a *S. equi* positive sample, our laboratory has successfully developed two real-time qPCR assays able to differentiate between field and vaccine *S. equi* strains. One hundred and seventy-one field samples from horses, which tested qPCR-positive for *S. equi*, were used for the validation of the differentiating assays. Twenty-two and 147 samples were consistent with the vaccine and field *S. equi* strains, respectively. One additional samples tested positive for both strains. All horses with detectable *S. equi* vaccine strain had a history of been recently vaccinated with the ML *S. equi* vaccine or in close contact with a recently vaccinated horse.

How does this research benefit horses? The ML *S. equi* vaccine is commonly used on endemic farms and during outbreaks of strangles. Since the ML vaccine strain of *S. equi* has retained some virulence and can cause mild disease, it is imperative to characterize a *S. equi* strain to determine its origin. The established and validated *S. equi* PCR assays, able to differentiate between field and vaccine *S. equi* strains, are available for the fine-tuning of molecular diagnostics in special conditions when a recently vaccinated horse develops strangles. Determining the *S. equi* strain type in a clinically infected horse is important to institute proper biosecurity protocols and characterize the source of the infection.



Investigation of the genetic make-up of equine coronavirus from foals and adult horses (Grant #19-13)

Investigators: Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine, Beatriz Martínez López, DVM, MPVM, PhD

Equine coronavirus (ECoV) is a newly recognized enteric virus of adult horses that has been associated with fever, lethargy and anorexia, as well as colic and diarrhea. Since 2010, clinical ECoV infections have predominantly been reported in adult horses. Data from our laboratory showed that the age distribution of confirmed ECoV infections was 20.5% in foals (age 0-6 months), 25.3% in horses aged 6 months to 5 years and 54.2% in horses older than 5 years. Usually, foals with clinical gastrointestinal disease are only positive for ECoV if other co-infections are present (e.g. rotavirus or *Clostridium perfringens*) with the prevalence of ECoV being similar between healthy and clinically affected foals. Adult horses with clinical signs experience a mono-infection with ECoV. Disease expression, as observed between foals and adult horses, may relate to various factors originating from the host or the virus.

In an attempt to determine if viral genetic factors are responsible for the observed age-dependent disease expression, our laboratory performed genetic sequencing of 40 individual ECoV strains from 9 young and 31 adult horses. Sequence comparison of the nucleocapsid (N) gene amongst the 40 strains of ECoV showed very high levels of homology, ranging between 97.9 to 99.0%. While geographic clusters of ECoV were determined, there was no marked difference of the N gene between strains originating from foals and from adult horses. The study results showed that age-dependent susceptibility to ECoV infection is not mediated by genetic differences of the N gene of ECoV and is more likely to depend on host factors.

How does this research benefit horses? ECoV has major clinical implications for the equine industry since it causes outbreaks with morbidity rates ranging from 15 to 85%. As with many viral infections, disease expression is often a multifactorial process, depending on host, viral and environmental factors. Determining risk factors is essential in order to establish proper preventive measures. While the study results showed that there are no genetic differences in the virus strong enough to account for the age-dependent disease expression of ECoV, it remains prudent to separate young from adult horses, as

foals have been shown to be subclinically infected and potentially act as a source of infection for older animals.

ORTHOPEDICS & LAMENESS

Bolstering tendon repair with mesenchymal stem cells that secrete biglycan (Grant #18-1)

Investigators: Michael Mienaltowski, DVM, PhD, Elizabeth Maga, PhD

Mesenchymal stem cells (MSCs) have been used in regenerative strategies to improve healing of tendon; they have been shown to have immunomodulatory effects and to serve as resources for trophic factors to bolster tissue healing. In order to study the effects of these cells using a lab-based assay, optimization of the current cell culture model is required. We hypothesized that transfection of expression vectors expressing small leucine-rich repeat proteoglycans (SLRP) like biglycan and decorin would bolster tenogenic properties of cells. However, after transfection with these plasmids, we found that adipose-derived MSCs did not express any higher levels of SLRPs than controls. Instead, the MSCs seemed to be stressed by the introduction of the plasmids. Because adipose-derived MSCs are injected into tendons alone, we recognize that they will interact with tendon proper and peritenon cells. Thus, we also examined the relationships between these tendon cells and the adipose-derived MSCs through co-culture of tendon cells with adipose-derived MSCs. In



co-culture, all three cell types – tendon proper cells, peritenon cells, and adipose-derived MSCs – exhibited gene expression profiles considered favorable for a tenogenic phenotype. That is, it appears that these cell types all secrete factors that promote tendon-forming features. Tenogenic transcription factors and extracellular matrix markers were most affected. In this study, we determined that application of expression vectors for SLRPs require further optimization and consideration of stresses to MSCs. Furthermore, adipose-derived MSCs, tendon proper cells and peritenon cells all interact in a manner favorable for tendon formation *in vitro*. It is likely that these positive interactions occur in the tissue as well.

How does this research benefit horses? Our findings highlighted the fragile nature of adipose-derived MSCs when it comes to cell manipulation – particularly the introduction of expression vectors to promote the secretion of extracellular matrix (tendon structural and regulatory proteins) – ahead of stem cell injection. Moreover, the co-culture research confirms utility of adipose-derived MSCs for bolstering tendon-forming expression profiles. This study helped to optimize our current *in vitro* model, which can now be used to systematically investigate the role of MSCs on tendon repair.

How do horseshoe traction features alter hoof grip on performance footings? (Grant #18-7)

Investigators: Christina M. Rohlf, Tara Doherty, DVM, Susan M. Stover, DVM, PhD, DACVS

The grip of performance surfaces is a risk factor for lower leg injuries of sport horses by affecting the extent of hoof slide and stability of the leg. Horseshoe traction features may modify surface interactions. Surface grip was measured with eight paired cadaver hooves on a dirt surface (sand) and a synthetic surface (sand with fiber). Hooves were shod with positive (low toe grab), neutral (flat), and negative (sliding plate) traction characteristics. Unshod hooves served as a control. Surface material had a greater effect than horseshoe traction characteristics on surface grip, with the synthetic surface exhibiting significantly higher grip than the dirt surface. Traction characteristics altered the shear force most notably on the synthetic surface, with sliding plates exhibiting lower grip than the unshod hoof. However, traction characteristics did not affect the grip

on the dirt surface. These results indicate that the addition of fiber alone to surface material can significantly alter the grip at the hoof-surface interface, while horseshoe traction features have a lesser effect on grip properties.

How does this research benefit horses? The choice of surface material and design of horseshoe traction features to improve grip have previously been driven by subjective opinions. This study scientifically quantified the effects of surface material and horseshoe traction features on performance factors, which directly affect the risk for leg injury in sport horses. Results of this study will inform horseshoe practices and guide the installation of surface materials which enhance the welfare and safety of performance horses.



**Aluminum Flat
Racing Plate**



**Aluminum Racing
Plate with 3.9mm
Toe Grab**



Sliding Plate



PET scans improve the detection of injuries in the horse foot when compared with MRI (Grant #18-13)

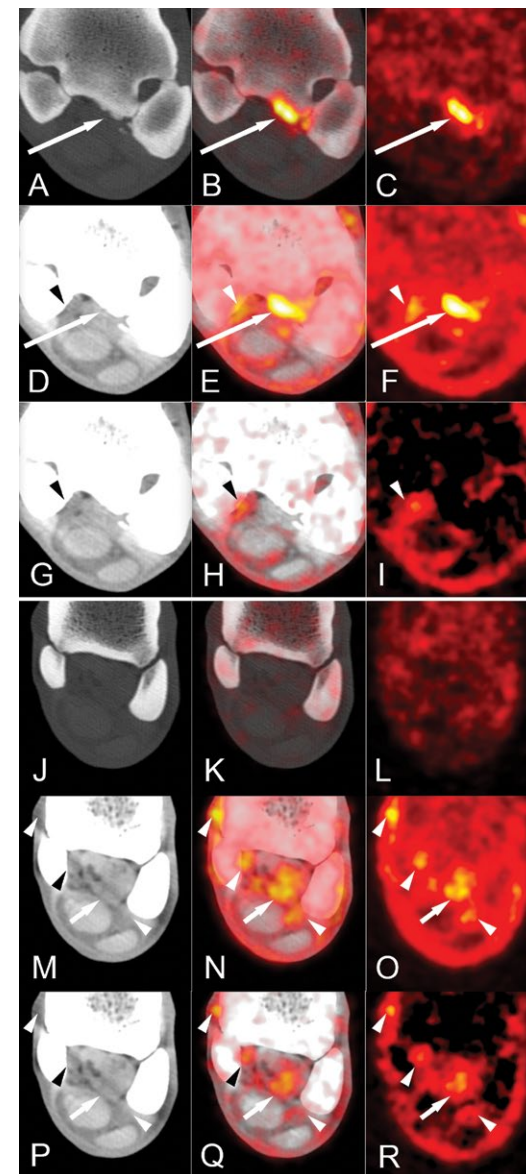
Investigators: Mathieu Spriet, DVM, MS, DACVR, DECVDI, DACVR-EDI, Jannah Pye, DVM, Larry Galuppo, DVM, DACVS-LA, Scott Katzman, DVM, DACVS-LA

MRI is the primary reference imaging technique used to investigate injuries responsible for foot pain in horses. However, MRI cannot explain the origin of the pain in some horses. Positron emission tomography (PET) is a new imaging modality that provides information about injuries by using a small amount of a radioactive dye. PET is able to recognize very early injuries and distinguish between active injuries and old scars. In this study, 12 horses that recently had MRI for investigation of foot pain were also imaged with PET. PET and MRI identified the same injuries in the majority of cases but there were a few situations where PET provided more information than MRI. These included:

- MRI typically only detects large bone bruises of the coffin bone, while PET is excellent at demonstrating even small areas with abnormal bone,
- The attachments of ligaments on bones can be challenging to evaluate by MRI. PET was very helpful at demonstrating abnormal marker accumulation, either in the bone or the soft tissue part of the ligament.
- Early arthritis is associated with small bone spurs that are challenging to recognize on MRI. As these developing spurs are actively growing, they display good PET marker accumulation, helping with their identification.
- MRI is excellent at identifying tendon injuries, but can be limited in its ability to distinguish active injuries from scar tissue. The soft tissue PET marker is excellent at distinguishing between the two, as it only accumulates within active injuries.

Figure 1: Images of the left hind suspensory origin (top 3 rows, A-I) and proximal aspect of the body of the suspensory (bottom 3 rows, J-R) of a 12-year-old Warmblood. A dual tracer ^{18}F -NaF and ^{18}F -FDG PET scan was performed. ^{18}F -NaF images (C, L) were obtained first. ^{18}F -FDG was then injected during the same anesthesia and combined tracer images (F, O) were obtained. The ^{18}F -NaF images were subtracted from the combined tracer images to obtain ^{18}F -FDG-like images (I, R). The left column displays CT images (bone window (A, J) and soft tissue window (D, G, M, P)), the central column shows PET/CT fused images. Lateral is to the left. There was marked focal increased ^{18}F -NaF uptake (long arrow) at the lateral plantar proximal aspect of the third metatarsal bone, visible in both ^{18}F -NaF (B, C) and combined ^{18}F -NaF / ^{18}F -FDG (E, F) images, at the attachment of the suspensory ligament, with associated contour irregularity on the CT, indicative of active enthesopathy. There was no abnormal ^{18}F -FDG uptake at the suspensory origin. The focal uptake adjacent to the second metatarsal bone (arrowhead) was vascular uptake. The bone uptake was not apparent on the subtracted images (H, I). There was moderate increased ^{18}F -FDG uptake at the lateral aspect of the body of the suspensory ligament (short arrow), associated with loss of

Figure 1.



normal architecture of the suspensory ligament on CT (M,P) appreciated on both the combined 18F-NaF / 18F-FDG (N,O) and the subtracted (Q,R) images. This indicated an active suspensory body desmitis. The arrowheads indicate incidental vascular uptake.

How does this research benefit horses? This study confirmed that PET is an excellent tool for imaging the horse foot to explain the cause of the lameness and plan appropriately for treatment. Depending on the type of injury expected, PET can be used in addition to MRI, but in some cases, PET can be used prior to or instead of doing an MRI. The development of equine PET has added a very powerful tool to help figure out foot lameness in horses.

This research was reported in the *American Journal of Veterinary Research* 2022;83(7): ajvr.22.03.0051.

PET scan improves the assessment of the hock and suspensory apparatus in lame horses

(Grant #18-22)

Investigators: Mathieu Spriet, DVM, MS, DACVR, DECVDI, Stefanie Arndt, DVM, Sabrina Wilson, DVM, Larry Galuppo, DVM, DACVS-LA, Scott Katzman, DVM, DACVS-LA, Marcos Perez Nogues, DVM, DACVS-LA

The hock and suspensory apparatus are two common sites of injuries responsible for hind limb lameness in horses. Distinguishing which of the two areas is responsible for the lameness can be challenging due to their proximity. These areas are commonly imaged with X-rays and ultrasound, but there is



sometimes limited association between the imaging findings and the clinical signs. Mild changes are common both with X-rays and ultrasound and may or may not be the source of pain. Positron emission tomography (PET) is a newly available imaging modality in horses that has the ability to detect subtle injuries and also distinguish between active and inactive injuries when changes are seen with other modalities. This study was the first to investigate the value of PET to assess both the bone and soft tissue changes in horses with pain localizing to the distal hock/suspensory area. The study confirmed that, in this population, changes could be seen in several regions. It was possible to distinguish horses with abnormalities in their hock joints, horses with abnormality in the attachment of the suspensory ligament on the cannon bone, and horses with changes in the suspensory ligament itself. There was high agreement between the three different observers assessing the images.

How does this research benefit horses? Dual tracer PET of the equine distal hock and suspensory apparatus is now used on regular bases to evaluate horses with pain originating from this region. The results of PET are very helpful for treatment and rehabilitation planning.

Evaluating the effect of footing properties on tendon and ligament strains in show jumping horses (Grant #19-07)

Investigators: Christina Rohlf, David Hawkins, PhD, Tanya Garcia-Nolen, MS, Susan M. Stover, DVM, PhD, DACVS-LA

Show jumping horses commonly injure tendons and ligaments in the lower limb, especially the suspensory ligament and superficial and deep digital flexor tendons. Due to limb anatomy, the amount of tendon and ligament stretching (strain) is affected by the amount of fetlock, pastern, and coffin joint extension during exercise. This study used high speed video to track fetlock, pastern, and coffin joint movement of four horses jumping a 1.1 meter parallel oxer on 12 different surfaces in northern California (5 dirt, 7 synthetic). The horses averaged 9.8 years of age and included 1 mare and 3 geldings. Average takeoff velocity was 5.97 m/s, with an average jump height of 1.27 m at the girth. Our

findings showed that extension of all three of these joints was significantly greater at landing than takeoff. Additionally, fetlock and coffin joint extension were greater on dirt than synthetic surfaces, while pastern extension was greater on synthetic than dirt surfaces. The reported surface effects on coffin and pastern extension were greater on the leading limb compared to the trailing limb.

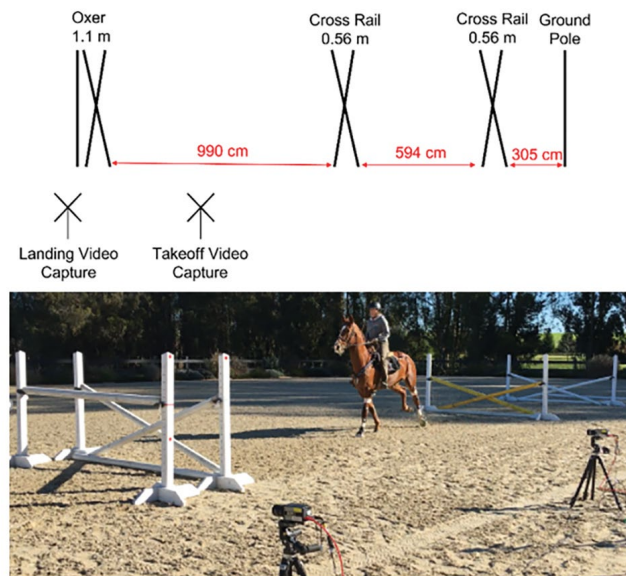


Figure 1. Scaled diagram of jumping grid (top) and photograph of jumping grid (bottom). Two high speed cameras were used to record takeoff and landing of the final 1.1 m oxer.



Figure 2. Marker layout for the forelimb.

How does this research benefit horses? These results help contribute to the scientific development of a set of standards for arena surface properties, designed to minimize tendon and ligament injuries of jumping horses. These standards would guide the construction and management of arena surfaces to reduce the risk of injury for horses that train and compete on such surfaces.

Assessment of bone growth in horse fetuses and newborn foals (Grant #19-23)

Investigators: Mathieu Spriet, DVM, MS, DACVR, DECVDI, DACVR-EDI, Catherine Renaudin, DVM, DECAR

Equine fetal growth is routinely assessed by ultrasonography using fetal growth measurements. Femur length and eye volume can predict gestational age in Quarter Horses up to 6 months of age with an accuracy of within 2 weeks. As pregnancy advances, age predictions are not as precise. This study aimed to evaluate a new fetal growth parameter: the first phalange (P1). The length of P1 was measured and P1 bone maturation was described by recording the time of appearance and closure of P1 secondary ossification centers. Correlation was assessed between ultrasonographic findings observed within the last 2 weeks of gestation and radiographic findings obtained at birth was evaluated. Data was obtained from 10 healthy Quarter Horse mares with known gestation dates that underwent transrectal ultrasound every 2 weeks from 9 months of gestation until

parturition (Figures 1 and 2). 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 (Figure 3). The proximal and distal ossification centers both appeared between 277 and 303 days of gestation (2 weeks). The proximal ossification



Figure 1. Transrectal ultrasonographic image of P1 in longitudinal view of a 245 days old QH fetus: P1 measures 24.5 mm (between +); no ossification center is seen.

center did not close as opposed to the distal one that closed between 306 and 333 days of gestation (2 weeks). All ultrasonographic findings were confirmed on radiographs, with the exception of the length of P1. As P1 becomes too long to be measured close to parturition, the latest ultrasonographic measurement is therefore underestimated.

How does this research benefit horses? We confirm that P1 length can be used as a novel fetal growth parameter. In addition to the other growth parameters already known, P1 length will improve the prediction of the 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 Quarter Horses that may be used in the future in the decision-making process of inducing parturition in the mare. It may help also identify risk of foal health issues at birth, such as prematurity or dysmaturity due to abnormal development.

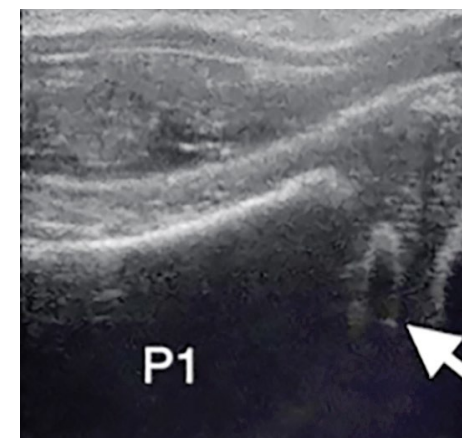


Figure 2. Transrectal ultrasonographic image of P1 in longitudinal view of a 301 days old QH fetus: proximal ossification center of P1 (arrow) is seen.

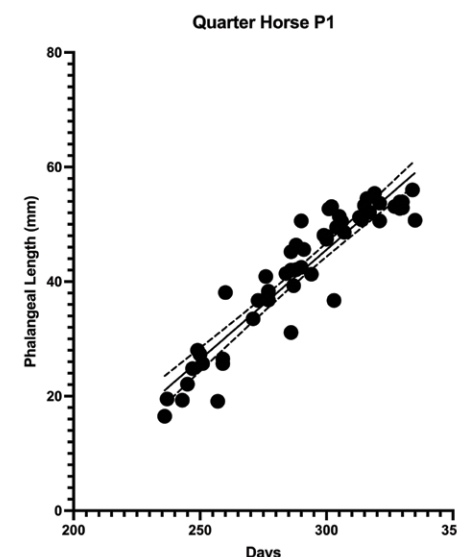


Figure 3. Growth chart P1 length versus gestation days.

REPRODUCTION

Ovarian hormones in follicular fluid (FF) are predictive markers of oocyte quality and maturation rates in mares (Grant #18-12)

Investigators: Stuart Meyers, DVM, PhD, DACT, Alan Conley, BVSc, MS, PhD, FRCVS, DACT, Alejandro de la Fuente, DVM, MS

The follicular fluid of antral follicles is part of the environment where an oocyte acquires its competence to become a healthy embryo. Molecules secreted by the mural granulosa cells (GC) and cumulus cells (CC) surrounding the oocyte are part of the signaling mechanism between the oocyte and its environment that control the development and maturation of the oocyte before ovulation. Anti-Müllerian hormone (AMH), Inhibin-B (Inh-B), and Inhibin-A (Inh-A) are important hormones secreted by GC and CC that exert effects not only in the follicle. However, their concentration in the follicular fluid of horses has not been characterized. In our study, we determined the concentration of AMH, Inh-B, and Inh-A in follicles ranging from 5-40 mm in size. We found that AMH presents a peak concentration in 15 mm follicles. Inhibin-B increases its concentration as the follicle grows. However, it presents a small decrease after the follicle reaches a size of 30mm. Inhibin-A concentration on the other hand, increases as the follicle grows without showing a decrease. Additionally, from the whole pool of follicles aspirated, size 10, 15, and 20 mm were the more abundant and we obtained a better oocyte recovery rate in follicles of size 15mm.

How does this research benefit horses? The goal of this study is to understand the hormonal regulation of follicle growth, to improve oocyte quality from growing follicles, and to increase fecundity of mares by improving embryo production. ICSI is an IVF technique that is becoming an important part of reproductive success in valuable horses. Understanding the factors controlling oocyte maturation will result in improved embryo development, thereby increasing pregnancy rates and production of healthy foals.

DNA sequencing of equine embryos for detection of chromosomal errors (Grant #18-14)

Investigators: Stuart Meyers, DVM, PhD, DACT, Ghislaine A. Dujovne, DVM, MS, DACT, S Chavez, Alejandro de la Fuente, DVM, MS

Early embryonic death in horses is costly and poorly understood, with higher loss rates in older mares and with advanced reproductive techniques. Detecting abnormalities in early development associated with later pregnancy loss would guide embryo selection and direct future research on causes of early embryonic death. Noninvasive imaging to precisely determine the duration of vital early embryonic events has allowed us to create the first predictive model of equine embryo development (Meyers et al, 2019; Table 1). Time-lapse imaging was used to develop a predictive model of success to blastocyst stage by identifying precise timing of cellular divisions and aberrations of embryo development. Chromosomal abnormalities were assessed by DNA sequencing in dividing embryos and indicate that cell division timing influences reproductive successes of horse embryos. DNA sequencing of embryos surviving to blastocysts has generated a complex of genes that we are currently studying that will be used to identify genes associated with developmental success, and targets for future therapeutic options. In the figures below, we show that equine embryos display varying characteristics that indicate abnormal cell divisions and fragmented DNA and chromosomes are associated with embryo failure and associated infertility.






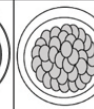
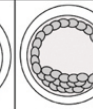
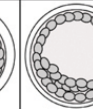
								
Embryo Stage	t0 Cytoplasmic Extrusion	t2	t4	t6	t8	morula	Blast with pulse	Expanded blastocyst
Initial Event (mean hrs.)	19.95	24.98	39.35	57.75	79.11	96.89	146.72	161.51

Table 1. A timeline of pre-mitotic and mitotic events post-fertilization by intracytoplasmic sperm injection of embryos which successfully developed to blastocyst stage.

After generating embryos *in vitro* using ICSI, noninvasive imaging key cell division times were marked and noted as seen in Table 1. Mitotic parameters were retrospectively analyzed in embryos that succeeded or fail to reach blastocyst stage to identify events in equine embryonic development that are predictive of early embryonic failure and death.

Using fluorescence staining, we have been able to identify precisely which cells in the developing embryo shows abnormal chromosomes and mitotic structures. In Figure 1, we have shown that normal- appearing embryo cells display very abnormal chromosomes and spindle structures when special fluorescence stains are used. The asterisks in Fig 1b below shows a very erratic pattern of chromosome defects with multiple unaligned (blue) chromosomes.

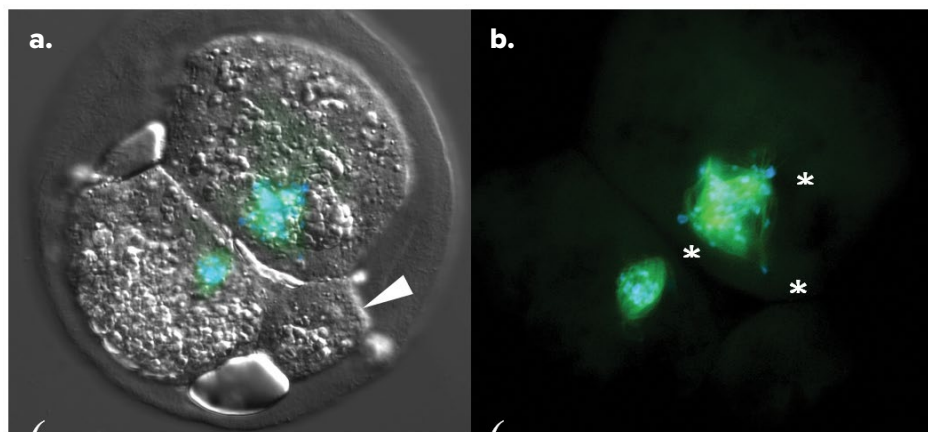


Figure 1. A horse embryo fixed and stained 18 hrs post ICSI. (a.) Phase contrast microscopy with immunofluorescence of tubulin using monoclonal anti-α-Tubulin-FITC antibody (green) and nuclear staining (blue) using Hoechst 33258 (b.) without phase contrast microscopy. The embryo had fragmented, resulting in a blastomere containing no DNA (white arrow) and did not exhibit cytoplasmic extrusion. Multipolar spindle formation can be seen, and white asterisks mark spindle poles.

Figure 2 is a comparison of the chromosomal status of embryos between 2-12 cell stages using single-cell sequencing. 11/16 embryos include at least 1 blastomere with chaotic aneuploidy, which is defined as having 5 or more chromosome losses and gains. Additionally, in 9/16 embryos, segmental

Euploid, aneuploid and segmental blastomeres within equine embryos following ICSI

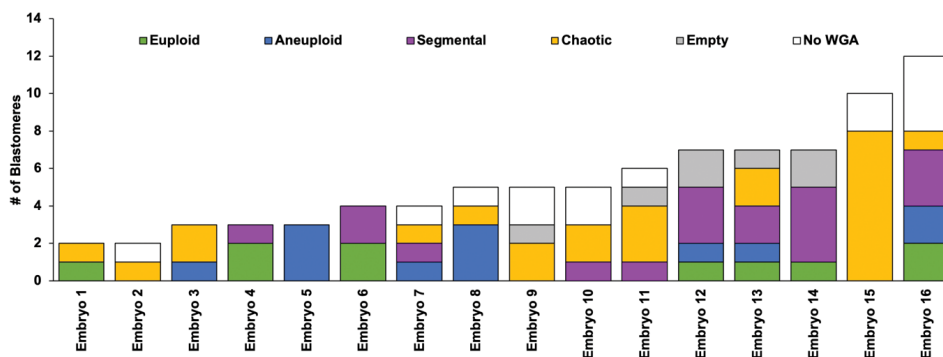


Figure 2. Ploidy status of 16 embryos determined by single-cell next-generation sequencing (WGA - whole genome amplification).

aneuploidy was detected where segmental deletions, duplications, and amplifications had occurred.

How does this research benefit horses? Assisted reproductive techniques (ART) in the horse industry are growing in clinical use and importance in breeding valuable mares. While the proportions of embryos that survive to blastocyst remains low, the significant cost of embryonic loss can be minimized by transferring high quality embryos of predicted success. The development of a set of markers of embryonic success will allow a deep understanding of equine embryo development, improve preimplantation genetic diagnostics, and result in birth of healthy foals.

Characterization of intracellular calcium (Ca^{2+}) stores in stallion sperm (Grant #18-17)

Investigators: Stuart Meyers, DVM, PhD, DACT, Gino Cortopassi, PhD

As the only method for long-term sperm storage, cryopreservation is widely used in the equine breeding industry, despite causing significant declines in fertility rates and sperm motility. Efforts to improve post-thaw motility are limited by a

critical gap in knowledge of the regulatory mechanisms of motility. Intracellular calcium (Ca^{2+}) signaling is known to be important for motility maintenance and is significantly altered by cryopreservation in stallion sperm. We confirmed the presence of ER-like Ca^{2+} stores in fresh stallion sperm by demonstrating dose-dependent Ca^{2+} release to thapsigargin (sarco/endoplasmic reticulum Ca^{2+} -ATPase (SERCA) inhibitor; Tg) treatment. The approximately 3-fold elevation in Ca^{2+} suggests that the ER-like Ca^{2+} stores are separate from other, larger intracellular Ca^{2+} stores, which could represent the acrosome. Additional work is needed to determine the intracellular localization of these ER-like Ca^{2+} , to investigate whether they are altered by cryopreservation, and their implications in sperm motility, mitochondrial function and fertility. The work has demonstrated that stallion sperm oxidative and mitochondrial functions are unique to the equine species among livestock species.

How does this research benefit horses? In demonstrating that equine sperm are biochemically unique among livestock species, this project could significantly improve our understanding of how cryopreservation affects sperm physiology. The work also provides an opportunity to enable rational development of drug, stem cell, or immunologic-based therapies that may prevent or reverse oxidative injury to sperm, or by other mechanisms that affect male fertility. Producers desire stallions to remain commercially viable for additional breeding seasons and additional production of healthy foals. This project could allow greater participation of stallions from various breeds and expand domestic and international shipping of semen.

This research was reported in *Reproduction in Domestic Animals* 2019;54(S3):22–28 and *Clinical Theriogenology* 2019;11(3):353–359.

The role of critical factors in equine egg maturation using time-lapse microscopy (TLM)

(Grant #19-08)

Investigators: Stuart Meyers, DVM, PhD, DACT, Ghislaine A. Dujovne, DVM, MS, DACT, Anna Denicol, DVM, MPVM, PhD

During oocyte maturation, the cumulus cells go through a process of mucification, which enables the cumulus oophorous to expand. *In vivo* processes like ovulation of oocytes, sperm capacitation, and fertilization depend upon

granulosa and cumulus cell expansion. During *in vitro* maturation of cumulus-oocyte complexes, cumulus expansion has been reported to be positively correlated with blastocyst rate in bovine oocytes, although never described for horses. However, the time needed for expansion is longer in the *in vitro* culture as compared to that of *in vivo* maturation. Moreover, the magnitude of expansion is greater in the latter. In this study, we matured individual horse cumulus-oocyte complexes *in vitro* using the Miri™ Time-Lapse microscopy system, which allowed us to measure the area of the cumulus every hour for a period of 24 hours for the first time. Then, cells were processed for RNA-sequencing to determine their gene expression. Our results indicate that the gene expression of cumulus cells from *in vitro* matured COCs present a low expression of genes related to expansion, extracellular matrix, collagen synthesis, and hyaluronic acid synthesis when compared to the gene expression of *in vivo* matured COCs. We are currently exploring all the genes that present different expressions and determine their correlation with the cumulus expansion rates.

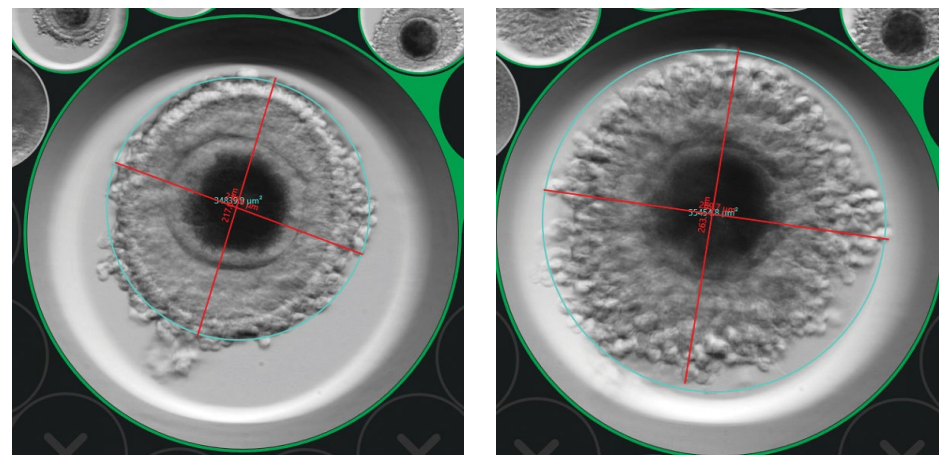


Figure 1. Images captured by the Miri™ time-lapse incubator. The area of the cumulus is being measured using the measurement tools incorporated in the Miri™ TL software.

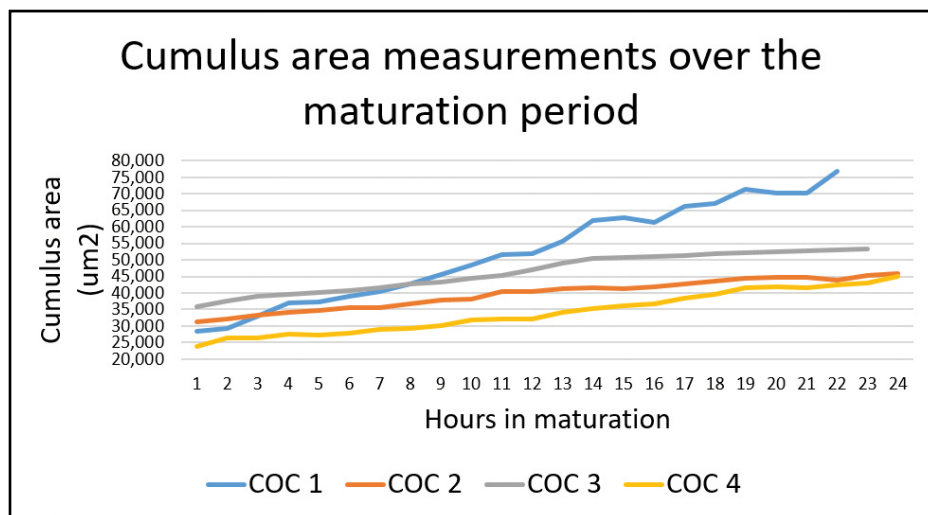


Figure 2. Line graph representing the increase in cumulus area measured hourly for a 24-hours period of Maturation culture in the Miri™ TL system.

How does this research benefit horses? Reproductive success of many horses depends on Assisted Reproductive Technology (ART). This study increases our understanding of factors regulating oocyte maturation. Potential benefits of this study include an improvement of *in vitro* maturation of oocytes, improving embryo production, and ultimately more healthy foals that otherwise would not have been produced.

This research is under review at *Reproduction in Domestic Animals*.

Predicting the 1st cell division of equine embryos using time-lapse imaging (Grant #19-09)

Investigators: Stuart Meyers, DVM, PhD, DACT, Candace Lyman, DVM, DACT, Ghislaine A. Dujovne, DVM, MS, DACT, Momoe Kato

This is a continuation of our study to develop a predictive model of successful embryo selection using a non-invasive time-lapse imaging embryo culture system. Previously, we tracked and defined cell cycle parameters establishing key morphological events leading to a successful embryo. In this study, we focused exclusively on the earliest stages of embryo development, which occurs post-fertilization but before first cell division. We identified two important and crucial events in this project related to the timing of the first cell division after fertilization: 1. the extrusion of cytoplasmic debris (called “cytoplasmic extrusion, CE”) and 2. reorganization of the fertilized zygote’s chromosomes and other nuclear content. We can now describe both of these events for horses for the first time based on the critical hypothesis that equine embryos have detectable mitotic landmarks of developmental competence by assessing the association between embryo morphology, developmental times, blastomere symmetry, ploidy status, and gene expression. These findings will help us gain a better understanding of equine embryogenesis, further improving early predictions that may lead to successful pregnancy outcomes.

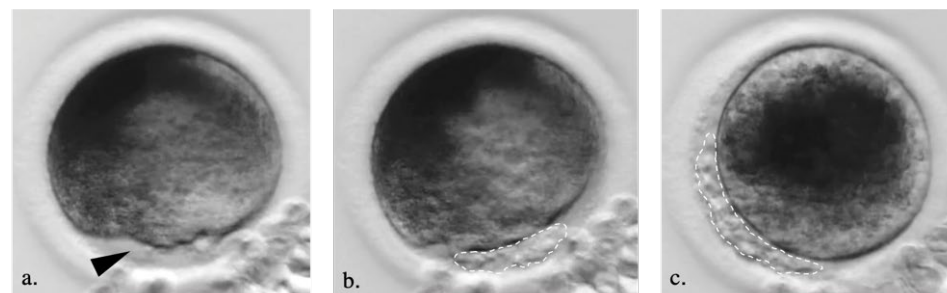


Figure 1. Cytoplasmic extrusion (CE) in the horse embryo. This sequence of images shows: (a.) the beginning of CE with the rippling of the ooplasm (black arrow), (b.) the cytoplasmic content beginning to be released into the perivitelline space (white dotted line), and (c.) the completion of CE with no more cytoplasmic content being released into the perivitelline space.

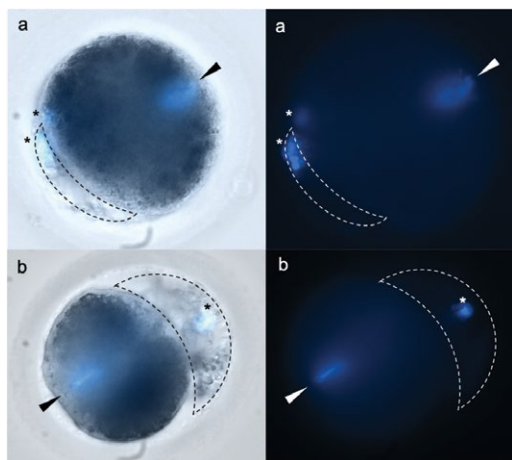


Figure 2. Zygotes stained with DAPI, which stains DNA, at (a) 20 hours and (b) 21 hours following ICSI. Cytoplasmic extrusion is outlined with a dotted line. Arrows show the formation of the metaphase plate opposite to the cytoplasmic extrusion. Asterisks mark polar bodies.

How does this research benefit horses? Assisted reproductive technology (ART) provides the ability to transfer embryos to produce genetically valuable horses. Abnormalities in early embryo development are crucial to understanding the causes of early embryonic death. Non-invasive imaging allows us to accurately determine key morphological events and the first predictive model of equine embryo development.

This research was reported in *Reproduction, Fertility and Development* 2019;31:1874-1884.

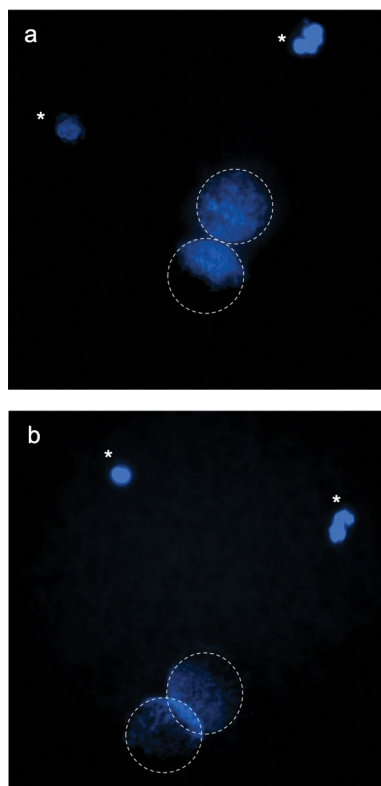


Figure 3. Zygotes (a, b) fixed and stained with Hoechst 33342 at 16 hours post ICSI showing uncondensed and condensing chromatin within pronuclei. Pronuclei are outlined with a dotted line. White asterisks mark polar bodies.

Baseline systemic and abdominal parameters after transvaginal aspiration of oocytes in mares

(Grant #19-11)

Investigators: Ghislaine A. Dujovne, DVM, MS, DACT, Daniela Orellana-Guerrero, DVM, DACT

Aspiration of oocytes (TVA) is critical for *in vitro* production of horse embryos. The procedure includes the aspiration of oocytes using a needle, which is guided by ultrasound from the vagina into the ovaries. Most mares recover uneventfully after the procedure, but others will develop complications including fever, bleeding and peritonitis. The goal of this study was to determine baseline information encompassing normal changes in blood parameters and changes in peritoneal fluid due to inflammation after the procedure. This study showed that all mares had some degree of inflammation in the peritoneal fluid 24 hrs after uneventful procedures with no changes observed in bloodwork at that stage.

This information will help clinicians to more quickly determine when further treatment is required following complications post-TVA.

How does this research benefit horses? This research provides clinically relevant information to evaluate optimal patient recovery after the procedure and be able to determine the plan of action in cases that have complications after aspiration of oocytes.

This research was reported in *Journal of Equine Veterinary Science* 2022;114:103949.

SURGERY/ANESTHESIOLOGY

Evaluation of a new pain reliever in horses with chronic lameness (Grant #18-18)

Investigators: Robert Brosnan, DVM, PhD, DACVAA, Alessia Cenani, DrMedVet, MS, DACVAA, Susan Stover, DVM, PhD, DACVS-LA, Tanya Garcia-Nolen, MS, Antonio José de Araujo Aguiar, DVM

RESIDENT GRANTS

3,4,4,4-tetrafluoro-3-(trifluoromethyl)-butan-1-ol (TFMB) is a novel analgesic discovered at the UC Davis School of Veterinary Medicine. A pilot study (16-02) in lame horses identified a TFMB route and dose range that caused no observable adverse effects. Drug administration was associated with improved lameness scores, improved pain scores, and increased step frequency, presumably due to less pain. However, the efficacy of TFMB compared to a standard treatment (positive control) and a placebo (negative control) needed to be evaluated.

The objective of this study was to measure subjective and objective measures of pain over time in horses with chronic orthopedic lameness following administration of TFMB, morphine (positive control), or saline (negative control) to determine if the pain-relieving effects of TFMB are as good, or better, and persists as long, or longer, than morphine.

Horses with naturally occurring static and chronic orthopedic disease received each of three treatments (TFMB, morphine, and placebo) in different orders with a 1-week drug washout period between treatments. Investigators unaware of the administered treatment performed analgesic assessments and orthopedic examinations over 24 hours to provide multidimensional comparisons of drug efficacy. Horses also wore pedometers to count the number of steps taken after each treatment.

Lame horses treated with TFMB walked significantly more for the first hour after treatment than the same horses after either morphine or saline control. However, by the 3-hour time point, step counts in TFMB horses returned to baseline whereas morphine-treated horse step counts were back to baseline by the 6-hour assessment time. Other subjective analgesia assessments (lameness and pain scores) were not statistically different between control, morphine and TFMB treatments.

How does this research benefit horses? TFMB provides effective analgesia in lame horses, with a duration of at least 1 hour but less than 3 hours for the dose and route studied. It is possible that this duration of effect may be extended with repeated dosing, and follow-up studies measuring drug concentrations after single and multiple doses in horses are currently underway. Nonetheless, even the shorter action of the single TFMB dose may be useful in acute pain scenarios, such as in horses recovering from anesthesia after surgery, where better analgesia may improve recovery quality and reduce perioperative injury risk.

MEDICINE & INFECTIOUS DISEASE

Comparing whether a horse's inflammatory response to West Nile virus vaccine is similar to their antibody-mediated response (Grant #19-26)

Investigators: Lauren Skipper, BVSc, Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

The purpose of this study was to establish if peak serum amyloid A (SAA) concentrations could be used to determine an appropriate immune response to a vaccine containing West Nile virus (WNV) antigen.

A pilot study was performed using 20 clinically healthy horses to identify peak SAA concentration post vaccination with a commercial multivalent WNV vaccine. Blood was collected at baseline and for up to 7 days post vaccination. After this pilot study, an additional 40 horses underwent the study protocol with SAA measurements collected before and 72 hours after vaccination. Ninety percent of the population of horses had an increase in SAA in response to WNV vaccination, although no significant correlation was identified between SAA peak and antibody titer fold changes. The main conclusions were that SAA was an unreliable predictor of immune response to WNV and is therefore not useful as a point of care test 72 hours following vaccination to determine adequate antibody response.

How does this research benefit horses? Antibody testing remains the gold standard method for determining vaccination response.

This research was reported in the *Journal of Equine Veterinary Science* 2021;106:103755.



Response of acute phase protein levels in healthy horses receiving injections with antimicrobials and anti-inflammatory drugs (Grant #20-23)

Investigators: Jurica Trsan DVM, Bridget Nottle, BVSc, DACVS, Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-Equine

Serum amyloid A (SAA), an acute phase protein, is a monitoring tool for acute infectious or inflammatory diseases in horses. SAA is often used to monitor complications post-elective procedures. With many postoperative horses receiving injections of antimicrobials and anti-inflammatory drugs, the goal of this study was to determine the response of SAA to these injectable medications in healthy horses. Six healthy adult horses were used in crossover design study, including one control and three treatment groups. The control group received no treatment, the procaine penicillin G (PPG) group received PPG only via intramuscular injection q12h for 72h, the flunixin meglumine group received flunixin meglumine only via intravenous injection q24h for 72h, and the combined treatment group received PPG (intramuscularly q12h for 72h) with flunixin meglumine (intravenously q24h for 72h). Whole blood was collected at 0, 24, 48, 72, 96 and 120 hours post-initial drug administration to measure SAA concentrations. The washout period between treatments was 30 days.

Individual SAA values were within the reference range of ≤ 20 $\mu\text{g/mL}$ for almost all horses in the control group. One control horse displayed a SAA value of 28 $\mu\text{g/mL}$ at 72 hours. All horses from the PPG group showed normal SAA values throughout the study. Except for one horse (SAA of 24 $\mu\text{g/mL}$ at 96 hours) from the flunixin meglumine group, all horses showed normal SAA values. For the PPG and flunixin meglumine group, 5 horses had SAA values within the reference range. One horse displayed SAA values from 32-45 $\mu\text{g/mL}$ between 48 to 96 hours post-drug administration. There was no statistical significance in area under the SAA time curve amongst control and three treatment groups ($P > 0.05$).

How does this research benefit horses? Local tissue injury caused by intramuscular PPG administration, intravenous flunixin meglumine or both does not elicit an inflammatory response that induces SAA values above the reference range in the majority of adult healthy horses. This information is important in order to determine that an increase in SAA is due to the infection and not medical treatment and/or the procedure.

ORTHOPEDICS

A novel fiberglass hoof casting technique for treatment of equine coffin bone fractures

(Grant #20-24)

Investigators: Shane Westman, SPF, GradDip ELR, Thomas Cullen, BVMS, DACVS, Thomas C Bergstrom, DVM, Lisa Edwards, DVM, DACVIM-LAIM, Tanya Garcia-Nolen, MS, Susan M. Stover, DVM, PhD, DACVS-LA

Coffin bone fractures in horses can be difficult to manage. Our team performed a study, using cadaver specimens from horses euthanized for other reasons, to test a fiberglass casting technique for coffin bone fractures. Our goal was to determine the effects on the size of the fracture gap under loading of the limb.

To perform this study, we first successfully used a novel methodology for creating minimally invasive coffin bone fractures in horse limbs while preserving all the collateral soft tissues. The limbs were then loaded using a biomechanical press and the effects on the fractures were assessed with radiographs. Our study showed that this fiberglass cast reduced the size of the fracture gap at the joint surface within the coffin joint and at other locations along the fracture when compared to non-casted feet.

How does this research benefit horses? Our results suggest that this technique could provide a very useful conservative treatment for coffin bone fractures in horses, negating the need for complex surgery and general anesthesia in some instances.



SURGERY

Comparison of tourniquet number for maximizing antibiotic concentration in horses undergoing intravenous regional limb perfusion (Grant #20-22)

Investigators: Thomas C Bergstrom, DVM, Isabelle Kilcoyne, MVB, DACVS, K. Gary Magdesian, DVM, DACVIM (LAIM), DACVECC, DACVCP, Jorge Nieto, MVZ, PhD, DACVS, DACVSMR

Joint infections in horses are serious medical conditions that may result in damage to the joint leading to career limiting lameness or even euthanasia of the horse. Intravenous regional limb perfusion (IVRLP) delivers high concentrations of antibiotics to a region of a horse's leg, including the associated joints, to treat infections. This procedure can be performed with one or two tourniquets to effectively isolate the area from the systemic circulation. In joints, such as the carpus (knee), there has been little research to determine if using a second tourniquet results in higher levels of antibiotics in the joint.

Our study compared the effect of IVRLP performed with one or two tourniquets on the concentration of antibiotics in a joint in the carpus. The results of the study indicate that there is no significant difference in peak antibiotic concentration when performing an IVRLP with one or two tourniquets. Similarly, the number of tourniquet(s) did not affect the time to peak concentration of antibiotic in the carpus. This finding indicates that a single tourniquet is sufficient to maximize antibiotic concentration when performing IVRLP in the carpus.

How does this research benefit horses? Data from this research will provide equine practitioners with information that will allow them to make informed decisions concerning how best to perform an IVRLP to deliver antibiotics to the equine carpus when treating orthopedic infections of that region.

This research was reported in *American Journal of Veterinary Research*. 2022;83(4):364-370.



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 –

Capabilities in equine sports medicine are enhanced significantly with the 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 the 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, Equine Ultrasound, and Equine Medicine Services.

J.D. Wheat Veterinary Orthopedic Research Laboratory – The J.D.

Wheat Veterinary Orthopedic Research Laboratory is an environment in which multidisciplinary studies pertaining to musculoskeletal disorders of animals and humans can be conducted. The goal of researchers participating in the laboratory is to understand the physiologic process of injury and musculoskeletal disease in performance, companion and production animals as well as in humans.

Kenneth L. Maddy Equine Analytical Chemistry Laboratory – The Kenneth

L. Maddy Equine Analytical Chemistry 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 two-fold mission includes expanding and disseminating new information regarding therapeutic medications in order to improve the welfare of California performance horses.

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 as a self-supporting unit of the UC Davis School of Veterinary Medicine. The laboratory is internationally recognized as a pioneer and expert in DNA-based animal testing. 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.

Veterinary Institute for Regenerative Cures – The UC Davis School of Veterinary Medicine is a national leader for veterinary regenerative medicine under the direction of the Veterinary Institute for Regenerative Cures. The institute has established laboratory techniques and animal models that have been used to study regenerative therapies for veterinary and human medicine. It has characterized equine stem cells isolated from different tissues (i.e. fat, bone marrow, umbilical cord blood and umbilical cord tissue) 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.





PUBLICATIONS

Drug Therapies



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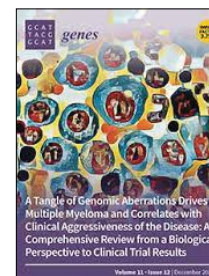


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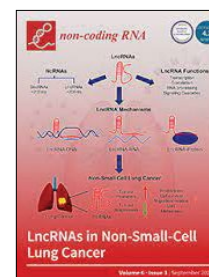
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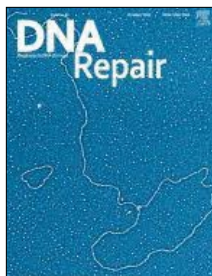
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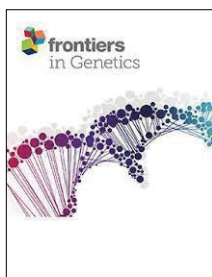
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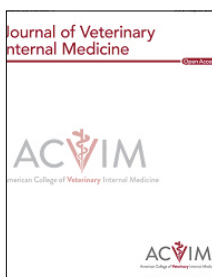


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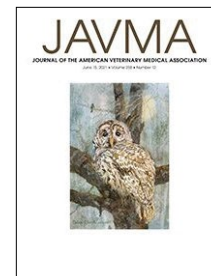
Medicine and Infectious Disease



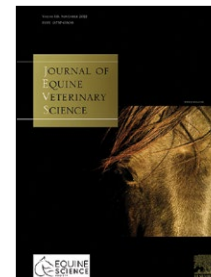
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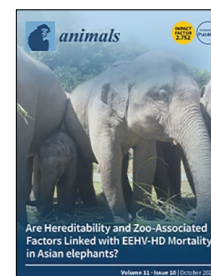
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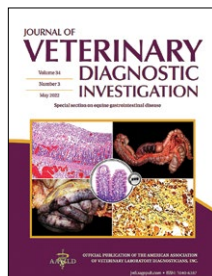
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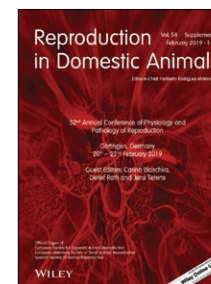
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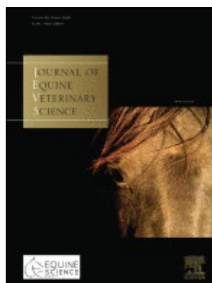
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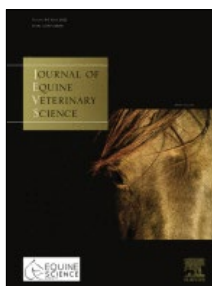
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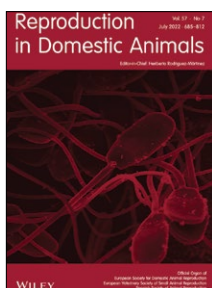
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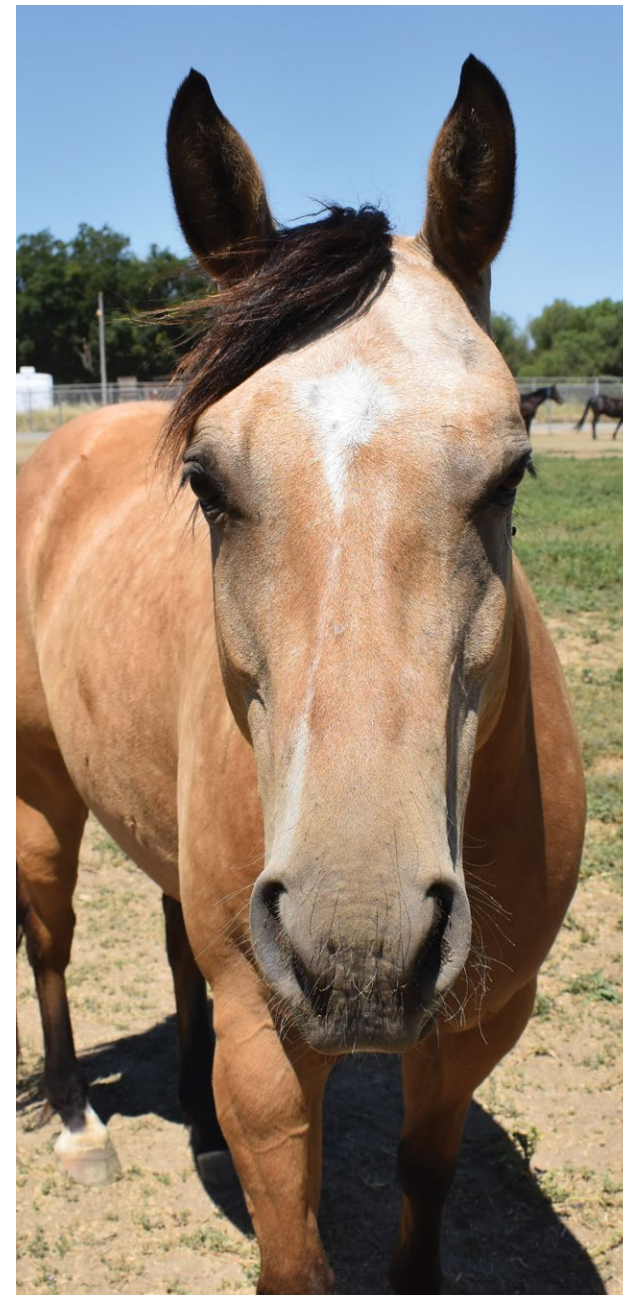
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NEWLY FUNDED RESEARCH STUDIES

- Genetic investigation of coat color and ocular phenotypes for the Pioneer Horse Health Project
- Incorporating long-read sequencing technology to improve the equine neuroepigenetic atlas
- A pilot study of intratumoral injections of interleukin-2 (IL-2) for equine melanomas
- Evaluation of vincristine chemotherapy for the treatment of lymphomas in horses
- Bolstering tenogenesis with Vitamin C supplementation
- Delivery of exogenous EGR1 mRNA to improve tendon formation
- Cardiac arrhythmia risk factors and prevalence in a mixed breed equine population
- Are equine oral squamous cell carcinoma lesions associated with equine papillomavirus?
- Investigation of newly discovered viruses in the nasal secretions of healthy and sick horses
- Investigation of the diagnostic accuracy of the serum to CSF antibody titer ratio against *Sarcocystis neurona* to support a laboratory diagnosis of equine protozoal myeloencephalitis
- Investigation of role of equids in the COVID-19 pandemic through serological and molecular testing
- Histologic examination and isolation of keratinolytic microorganisms involved in equine white line disease
- Elucidation of effective antibiotic treatments for equine *Corynebacterium pseudotuberculosis* infections using longitudinal comparative population genomics
- Antibody response and antigen detection of EHV-1 in horses following intranasal vaccine administration
- Epidemiological investigation of contemporary outbreaks of equine herpesvirus myeloencephalopathy
- Investigation of the detection frequency of H752 EHV-1 genotype in diagnostic samples (2016-2021)
- Genomic characterization of contemporary EHV-1 strains from outbreaks in North America
- Creating the infrastructure to integrate artificial intelligence into clinical decision-making
- Machine supported interpretation of laboratory data from diseased horses using unsupervised learning
- Does inhibition of centrally-acting catecholamines cause fentanyl to decrease isoflurane MAC in horses?

- 
- Pharmacokinetics of morphine and metabolites following oral administration: a new investigation of an old drug
 - Diagnostic and prognostic value of serial measurements of procalcitonin and sCD14+ in septic neonatal foals
 - Pharmacokinetics and biocompatibility of a novel cyclosporine-loaded microsphere thermo-responsive hydrogel drug delivery system in horses
 - Effect of furosemide on comprehensive renin-angiotensin-aldosterone system activity of horses
 - Determination of synovial fluid morphine concentration in the radiocarpal joint following IVRLP
 - PET imaging of the racehorse fetlock after surgical repair of fracture
 - Calibrating a model of racehorse proximal sesamoid bone stress-fractures for injury prevention
 - Investigating the timing, magnitude, and duration of muscle activation in the equine forelimb during jumping
 - Leading limb and hoof contact effects on hindlimb kinematics and hoof translation in show jumping horses
 - Regulation of gene expression in the equine placenta; what makes the placenta function?
 - Elucidating host-pathogen interaction in the equine placenta during nocardioform placentitis
 - Can cumulus cells during *in vitro* maturation predict successful fertilization and embryo development in horses?
 - Gene expression of equine cumulus cells during oocyte maturation: *in vitro* and *in vivo* conditions
 - Selection and characterization of high-quality stallion sperm using microfluidics and sperm cell membrane charge
 - Regulation of placental angiogenesis in equine pregnancies generated by somatic cell nuclear transfer
 - Equine placentitis: a new approach to understand an old problem
 - Pain assessment during and after TVA in mares using epidural and injectable analgesics
 - Establishing and characterizing a primary equine cumulus cell culture as a model for oocyte maturation

CENTER FOR EQUINE HEALTH RESEARCHERS



Verena Affolter, DVM, PhD, 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 chronic progressive lymphedema in horses.



Monica Aleman, MVZ, PhD, 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, chief of the equine internal medicine service, 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, PhD

Dr. Rebecca Bellone earned her PhD 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

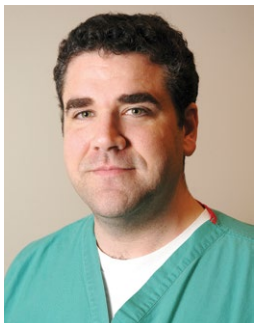
an Associate Adjunct Professor in the Department of Population Health and Reproduction and is the Director of the Veterinary Genetics Laboratory, a unit of the UC Davis School of Veterinary Medicine with an international reputation as experts in veterinary genetic testing.



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. Dr. Berryhill is 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, PhD, DACVAA

Dr. Robert Brosnan earned his veterinary degree from the UC Davis School of Veterinary Medicine in 1999, and a PhD 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, PhD

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.

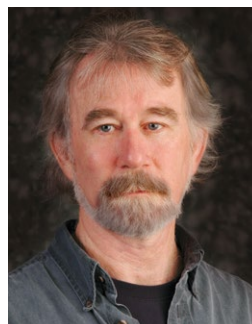


Alessia Cenani, DrMedVet, MS, DACVAA

Dr. Alessia 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, PhD, FRCVS, DACT

Dr. Alan Conley is a professor 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, PhD, PhD, DECAR, DACT

Dr. Pouya Dini is an assistant 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. Ghislane 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, PhD, 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 an associate professor in the Department of Population Health and Reproduction.



Larry Galuppo, DVM, DACVS-LA

Dr. Larry Galuppo is a professor 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., PhD, DECVF

Dr. Stefan Keller is an assistant 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, PhD, 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 of 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, PhD

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 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, PhD, DACT

Dr. Stuart Meyers, a professor 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, PhD

Dr. Michael Mienaltowski earned his DVM degree from Michigan State University in 2004, followed by his 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, PhD, 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 extracellular proteins play in tissue degeneration and disease prediction.



Nicola Pusterla, DVM, PhD, DACVIM, DAVDC-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, PhD

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 assistant 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 College of Veterinary Medicine. His research focuses on monitoring respiratory function during anesthesia, including linear and nonlinear models of respiratory mechanics, volumetric capnography, and electrical impedance tomography, 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 an associate 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, PhD, DACVS-LA

Dr. Susan Stover is a professor in the Department of Surgical and Radiological Sciences and director of the J.D. Wheat Veterinary Orthopedic Research Laboratory at the UC Davis School of Veterinary Medicine. 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, PhD, 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.



Katherine Watson, DVM, PhD, DACVP

Dr. Katherine Watson is an assistant 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, PhD

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.



CENTER FOR EQUINE HEALTH

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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

A photograph of three horses grazing in a lush green field. Two brown horses are in the foreground, and a white horse is further back. The background is a dense forest of green trees.

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 PIONEERING APPROACH TO EQUINE HEALTH

Horses are individuals, and a one-size-fits-all approach to their care can fall short in producing desired outcomes. **The Pioneer 100 Horse Health Project (P100HHP)** aims to lay the foundation for tailoring veterinary medical approaches to each horse's specific needs through precision medicine.

Precision medicine is a way to target diagnostics and treatments based on a patient's specific genetic, biomarker and phenotypic characteristics. The Precision Medicine Initiative, launched in 2015 to advance these approaches in people, resulted in targeted therapies for cancer and other conditions.

Thanks to advanced molecular tools, there is now the potential to apply precision medicine to horses. Genetic data and other biomarkers can be used to tailor medical treatments to an individual horse's genetics, its environment, and the interactions between the two.

The UC Davis Center for Equine Health, through support from Platinum Performance and the Alamo Pintado Foundation in memory of Dr. Doug



Dr. Callum Donnelly (L) and graduate student Myles Hammond perform a cardiac evaluation on a Pioneer 100 Horse Health Project horse.

Herthel, have developed the P100HHP, a first-of-its-kind precision medicine study in horses. This population of horses is the only dedicated group of research animals maintained for systems biology-based investigation of health and disease traits. The goal is to create a scientifically sound wellness program using a combination of multi-omics (genomics, proteomics, metabolomics, etc.) approaches focused on disease prevention. Data from this project could help evaluate, for example, how a particular patient is likely to respond to one medication versus another, making it possible to target treatments for the most successful outcomes.

The P100HHP has gathered extensive data on 100 CEH teaching herd horses. These horses live at the center, having been donated for various reasons. The advantage of utilizing this population is that we have access to their medical records and can control many aspects of their environment, such as their diets, limiting variables in a way that would not be possible if the horses were housed in different locations. In addition, the majority of these horses are long-term CEH residents, meaning that researchers can follow their health and associated data over time (deep longitudinal phenotyping).

Dr. Carrie Finno, CEH Director, leads these scientific efforts through her research laboratory. From 2020-2022, Dr. Callum Donnelly, a PhD student in Dr. Finno's laboratory, performed extensive data collection on these horses. Additionally, collaborations with other UC Davis faculty, including Drs. Rebecca Bellone, Jessica Morgan, Heather Knych and Emily Berryhill have furthered these efforts. To date, every P100HHP horse has undergone:

Extensive Phenotyping

- Medical and nutritional records
- Reproductive history for mares and stallions
- Vaccine history and responses
- Physical examinations/weight/body condition score/height
- Coat colors, patterns, and markings
- Lameness examinations (twice a year for two years)
- Neurologic evaluations (twice a year for two years)
- Testing for Equine Metabolic Syndrome (twice a year for two years)
- Full ophthalmic and cardiac evaluations
- Fecal egg counts (twice a year for two years)

- CBC, chemistry, lipid profile (once a year for two years)
- Vitamin and mineral panel
- Testing for Cushing's Disease (twice a year for two years)
- Blood typing

Multi-omic Profiling

- Whole genome sequencing (20X coverage)
- Mammalian methylation array profiling (in collaboration with the Horvath laboratory at UCLA)
- Plasma metabolome profiling (twice a year for one and a half years)
- Fecal microbiome profiling (twice a year for two years)
- Targeted proteomic profiling of plasma and cerebrospinal fluid (CSF)

With this wealth of phenotypic and -omics data, researchers have begun to:

- Develop an “aging clock” for horses based on the epigenetic markers of DNA methylation
- Define horses with “high” and “low” intestinal parasite burdens and examine the underlying genetics that influence these traits
- Identify subtypes of equine metabolic syndrome (EMS) and identify associations between fecal egg count, fecal microbiome and EMS status
- Investigate the overlap between EMS and equine Cushing's disease
- Identify new genetic variants for coat colors
- Determine new biomarkers of equine neurologic diseases
- Investigate the genetics of drug metabolism in horses
- Identify blood metabolite changes that precede changes on routine bloodwork
- Define the role of nutrition and metabolic status in shaping the fecal microbiome

The P100HHP project highlights a tremendous contribution of our UC Davis horses to “pioneer” the field of equine precision medicine. Consequently, subsequent development of targeted diagnostics and therapeutics will be able to be **tailored to a specific equine patient** and increase our success in managing difficult diseases.

We invite you to stay connected with CEH to learn about the diverse outcomes from the P100HHP in the coming years!



Dr. Carrie Finno (L) and Dr. Callum Donnelly (R) weigh one of the horses on a scale as part of the phenotypic data collection.



Lameness examination on a Pioneer 100 Horse Health Project horse.



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



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