



ORTHOPAEDIC RESEARCH CENTER

2023 ANNUAL REPORT



ORTHOPAEDIC RESEARCH CENTER

PROGRAM HIGHLIGHT

Equine Sports Medicine and Rehabilitation

Read more on page 36



Mission

To investigate the pathogenesis, diagnosis, treatment and prevention of neuro-musculoskeletal disease and injury for the advancement of both animal and human health.

Purpose

To find holistic solutions to neuro-musculoskeletal problems, addressing restoration of function, repair of injury, and reduction of pain.

Philosophy

To develop innovative research strategies that elevate the standard and quality of patient care, with continued critical assessment of our results, and to use these novel findings to guide management of neuro-musculoskeletal diseases.

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LETTER FROM THE DIRECTOR

Laurie R. Goodrich, D.V.M., M.S., Ph.D.
Barbara Cox Anthony University Chair in Orthopaedics



This annual report is another testament to our Orthopaedic Research Center program, its people, our collaborators, and funding partners, as well as our philanthropic supporters. The report reflects the incredible impact of our amazing team and the research that they carry out to help horses and people. I am hoping you will agree that when you look through the pages of this report, Year 2023 was extremely productive and the fruits of our labors can be found throughout as published manuscripts, research abstracts, and presentations given at both national and international conferences. The productivity of our clinician scientists, graduate students, and staff reflects their dedication and resolve in finding solutions to difficult problems even in the face of recovering from the post-COVID budget and staffing issues that plagued the world globally.

In this issue we highlight a very special group of clinician scientists who make up the Sports Medicine and Rehabilitation service. They are actively working towards solving some of the most pressing sport horse problems in neuromuscular disease and injury prevention. They are also an incredibly hardworking group with intense dedication to their careers. Interestingly, they are all equestrians themselves which makes many of their major

pursuits in sports medicine and rehabilitation very personal. In fact, many of the images throughout this Annual Report feature them either working on their patients to return them to athleticism or participating in sport horse events and competitions with their own horses. The American College of Sports Medicine and Rehabilitation, as you will read in the focus article on page 36, began by a group of clinician scientists across the country (including many from the ORC). The founders recognized the importance of initiating and expanding a specialty where there was an intense need to establish standards of care and to carryout research in areas where there was yet to be a focus but significant gaps existed. Interestingly, there are so many parallels in musculoskeletal injuries (and their treatments) between what our equine sports medicine patients and human athletes, that our MD counterparts whom we have close collaborations with, use what our research is revealing and apply it to their human patients. This underscores the horse being an excellent example for what therapies can benefit humans. This results in impactful translational research between horses and humans, which is the founding principle of our ORC program and the initiation of the C. Wayne McIlwraith Translational Medicine Institute. The clinician scientists within the ORC are also training the next generation of clinicians and researchers, of which there are three residents in training (one for each year of a three-year residency). These individuals will receive their Master of Science, and some will stay on to complete a PhD following their residency. This further pushes the forefront of research in this important arena and prepares those individuals for academic positions.

Also in this issue is a focus article on a previous trainee (in equine surgery and lameness), Dr. Lynn Pezzanite, who is a shining example of a successful member of our program. As you will read, Dr. Pezzanite completed her equine surgery residency, Master of Science, and then PhD and has now been hired into a tenure track position with the ORC/TMI program within the Department of Clinical Sciences. She is reaching new levels of research in the molecular science of osteoarthritis and immunology. Dr. Pezzanite also closely collaborates with individuals at the University of Colorado Medical School Program and has forged outstanding academic ties with them in turn leading to highly translational discoveries. Dr. Pezzanite is now further training DVM and graduate students and preparing them for "the next" generation. The legacy continues.

I hope you are inspired by the people and the work in this report. Every picture in this report features one of our staff, graduate students, or clinician scientists (including the cover picture). You will see in these images and in the work they produce, that they truly live the life they focus on both in work and at play. They inspire me every day and I am truly grateful to work with this team. Thank you to all of you that are supporters of our program. We could not accomplish what we do without you. I hope you enjoy this report, and I am always open to ways of improving what we do and how we report it. Please feel free to reach out any time.

Respectfully and in gratitude,

ORC TEAM

Faculty/Principal Investigators

Laurie Goodrich – Director of ORC, Barbara Cox Anthony University Chair in Orthopaedics, Professor of Equine Surgery & Lameness

C. Wayne McIlwraith – University Distinguished Professor, Founding Director of ORC, Barbara Cox Anthony University Chair in Orthopaedics Emeritus

Myra Barrett – Associate Professor, Veterinary Diagnostic Imaging

Luke Bass – Associate Professor, Equine Field Service

Erin Contino – Associate Professor, Equine Sports Medicine & Rehabilitation

Felix Duerr – Professor, Small Animal Orthopedic Medicine & Mobility

David Frisbie – Professor, Equine Sports Medicine & Rehabilitation

Kevin Haussler – Associate Professor, Equine Sports Medicine & Rehabilitation

Fiona Hollinshead – Professor, Small Animal Reproduction

Christopher Kawcak – Iron Rose Ranch Chair, Professor of Equine Surgery & Lameness

Melissa King – Professor, Equine Sports Medicine & Rehabilitation

Lauren Luedke – Assistant Professor, Equine Surgery & Lameness

Brad Nelson – Assistant Professor, Equine Surgery & Lameness

Yvette Nout-Lomas – Associate Professor, Equine Internal Medicine

Lynn Pezzanite – Assistant Professor, Cellular & Molecular Biology

Kelly Santangelo – Associate Professor, Microbiology, Immunology, and Pathology

Katie Seabaugh – Associate Professor, Equine Sports Medicine & Rehabilitation

Kurt Selberg – Associate Professor, Veterinary Diagnostic Imaging

Katie Sikes – Assistant Research Professor, Preclinical Surgical Research Laboratory

Lauren Smanik – Assistant Professor, Equine Emergency & Critical Care

Melinda Story – Leslie A. Malone Presidential Chair, Assistant Professor, Equine Sports Medicine & Rehabilitation

Kelly Zersen – Imaging/ Anesthesia Coordinator

Postdoctoral and/or Graduate Students

Charlie Barton – Resident and MS Candidate, Equine Surgery & Lameness

Taryn Boxleitner – DVM Candidate

Kate Bukovec – Resident and MS Candidate, Equine Sports Medicine & Rehabilitation

Sandro Colla – Resident and MS Candidate, Equine Sports Medicine & Rehabilitation

Angie Esselman – Resident and MS Candidate, Equine Sports Medicine & Rehabilitation

Gabi Kawahisa Piquini – Resident and MS Candidate, Equine Surgery & Lameness

Tom O'Brien – Resident and MS Candidate, Equine Surgery & Lameness

Frances Peat – PhD Candidate, Equine Sports Medicine & Rehabilitation

Gabby Solum – Resident and MS Candidate, Equine Sports Medicine & Rehabilitation

Riley Thompson – Postdoctoral Candidate, Equine Reproduction

Mikala Vig – Resident and MS Candidate, Equine Sports Medicine & Rehabilitation

Zoe Williams – Resident, Equine Sports Medicine & Rehabilitation

Machiel Ysebaert – Resident and MS Candidate, Equine Surgery & Lameness

Research Scientists and Staff

Michelle Alexander – Administrative Assistant, Equine Sports Medicine & Rehabilitation

Becca Cedar – Veterinary Technician, Equine Sports Medicine & Rehabilitation

Jennifer Daniels – Research Trials Coordinator

Brigita Fiske – Research Associate

Skylla Hall – Program Coordinator

Natalie Lombard – Surgical Technician

Melinda Meyers – Research Assistant, Equine Reproduction

Meredith Park – Veterinary Technician, Equine Sports Medicine & Rehabilitation

Nikki Phillips – Laboratory Manager

Shelby Roberts – Veterinary Technician, Equine Sports Medicine & Rehabilitation

Ryan Shelton – Lead Veterinary Technician

Taylor Winther – Laboratory Assistant

HISTORY

The Orthopaedic Research Center began as a multidisciplinary equine program dedicated to finding methods to treat and prevent equine musculoskeletal disease and injury. Prior to 1984, the program's research was primarily clinical. During this time, many of the techniques for arthroscopic surgery were developed and optimized at CSU, and these techniques were used to treat joint problems more effectively and, further, enable continued athletic function of equine athletes.

We also identified and defined a number of new clinical conditions and documented some of the best methods for diagnosis and treatment for musculoskeletal conditions. The goals of our program are summarized in our research focuses. As we developed arthroscopic surgical techniques to treat these clinical conditions, we identified limitations in terms of secondary osteoarthritis and articular cartilage loss, and this led into phase two of our program of finding

solutions through scientific research. A major goal of the program has always been to find solutions to musculoskeletal problems, especially joint injuries and arthritis. As clinicians, clinician scientists, and/or basic science researchers, we strive to offer the best possible treatment of clinical cases with continual and critical assessment of the results, which are then used to modify treatments and direct the research toward disease prevention. The program's goals are to use state-of-the-art research techniques to find new methods to rehabilitate musculoskeletal injuries, specifically damaged joints, tendons, and bones, to prevent or decrease the occurrence of joint disease and musculoskeletal injuries. We strive to improve methods of early detection, develop better treatments to prevent permanent damage to injured joints, and validate manual therapies and rehabilitation techniques.

The ORC collaborates closely with the Orthopaedic Bioengineering Research Laboratory, and we often function as a single unit. The ORC and OBRL, together with the Preclinical Surgical Research Laboratory and Orthopaedic Oncology, make up the Musculoskeletal Research Program, which is a Program of Research and Scholarly Excellence at CSU. This designation of PRSE to us was originally granted in 2004 and has been renewed in 2008, 2012, and 2016. The significant collaborations with the College of Engineering and School of Biomedical Engineering, as well as the Department of Health and Exercise Science, has added considerably to our research strengths. In recent years, considerable human-based funding— Orthopaedic Foundation, National Institutes of Health, Department of Defense, and corporate grants— has added to our support.

Another significant addition to the ORC has been the development of the equine ambulatory sports medicine and rehabilitation service and an Equine Sports Medicine and Rehabilitation Residency Program. This followed the accreditation of the new American College of Veterinary Sports Medicine and Rehabilitation specialty and four of our faculty being made charter diplomates. We quickly developed an

equine ACVSMR residency program and have added four diplomates (board-certified in American College of Veterinary Sports Medicine and Rehabilitation, equine specialty) to make us the largest Equine Sports Medicine and Rehabilitation Program in the U.S. This has led to considerable clinical and research advancements in the rapidly emerging field.

In 2016, we achieved funding of \$70 million to build the C. Wayne McIlwraith Translational Medicine Institute. This building came to fruition in 2018, and the Orthopaedic Research Center program moved into the TMI building at that time. The Gail Holmes building has now transitioned to be the Equine Sports Medicine and Rehabilitation Center led by Dr. Melissa King. The TMI is taking us to a new level of orthopedic research in translational musculoskeletal research (as well as allied areas of biologic therapies and stem cell research), doing what we have always done for horses but greatly expanding our efforts in human musculoskeletal disease. This is made possible by a lead gift of \$40.5 million from John and Leslie Malone for the building (an additional \$10 million in operating funds), \$10 million from CSU, and a \$20 million matching gift from Princess Abigail K. Kawānanakoa of Hawaii.



PROGRAM

Our Impact as a Preeminent Equine and Translational Orthopaedic Research Program

Both nationally and internationally, the ORC provides critical new findings of significant clinical impact and has been able to attract talented students who wish to pursue careers in orthopedic research. Students choose this program because of its excellent reputation and because of the opportunities they have to be involved in research during their undergraduate and pre-veterinary programs, and veterinary or post-veterinary careers (either while in residencies or post residencies). Many pre-veterinary students have served as volunteers in equine orthopedic research over the past 10 years; this allows students to develop a high level of research expertise during this undergraduate experience. This involvement encourages students to pursue advanced degrees and ultimately research careers. Our program also impacts undergraduate and pre-veterinary education by applying findings from research studies to clinical veterinary medicine.

The breadth of dissemination of information from the ORC is extensive, with information distributed to graduate and undergraduate students in eight departments within five colleges at Colorado State University. Many faculty members from these five colleges who are participants in the Orthopaedic Research Program are internationally recognized; they are therefore able to share research findings worldwide to the academic community, the equine industry, the scientific community, and private biomedical industry. The ORC's extensive collaboration with M.D.s doing research on similar areas of the musculoskeletal system, such as those at CU School of Medicine, Rush Medical Center, Stanford Medical Center, and Steadman Philippon Research Institute, as well as biotechnology companies, with collaboration in multiple NIH and Department of Defense research grants, has significantly impacted the treatment of humans with orthopedic injuries and osteoarthritis. Human medicine, as well as veterinary medicine, has been positively affected by the dissemination of the ORC's findings over the last several decades.

Impact of the Orthopaedic Research Center within the Translational Medicine Institute

Faculty and Staff: Over the last 25 years, funding for our orthopedic research and specialized personnel availability has increased dramatically. Until 1994, orthopedic research was being performed by faculty members within the Department of Clinical Sciences. The ORC research team now encompasses 25 full-time faculty members (including three bioengineering faculty) in our program. To support the work of faculty researchers, we now have 12 research associates/research trial coordinators/administrative assistants. We have 13 graduate students in the program as of 2023. To view the full list of ORC members, affiliates, graduate students, and postdoctoral candidates, please visit our website for their bios and publications (www.vetmedbiosci.colostate.edu/orc). Our current funding is approximately \$2 million to \$4 million annually.

Facilities: In 2002, thanks to generous private donors, most notably Gail Holmes and Herbert Allen, the construction of the Gail Holmes Equine Orthopaedic Research Center and the remodeling of the Orthopaedic Research Laboratories were completed with joint funding from the ORC, School of Biomedical Engineering, and vice president of research at the time, Dr. Tony Frank. At the same time, we built a state-of-the-art equine MRI facility (the first equine-dedicated MRI in the U.S.), funded by Ken and Virginia Atkinson together with a College Chair to fund personnel (that also involved a significant contribution from Jon and Abby Winkelried). In 2018, with the completion of the C. Wayne McIlwraith Translational Medicine Institute, the Orthopaedic Research Center program moved into the TMI building along with the imaging efforts that were initiated in the Gail Holmes building. This allowed access to new surgical facilities, a new gait laboratory, high-speed treadmill, and equine barns for our preclinical investigations to be performed. The gait laboratory and equine barn are part of the ORC program and the building, which houses both the gait lab and the new barn, is called the Equine Performance Analysis Facility.

The Gail Holmes building that once housed the ORC program is now dedicated to the Equine Sports Medicine and Rehabilitation Program, and the Orthopaedic Research Laboratories have received further renovation and are largely occupied by the OBRL. This space is shared, to some extent, with the ORC. These facility updates have greatly contributed

to the larger vision of the ORC mission of impacting not only horses but also people through translational research.

Endowed Chairs: The ORC has three, \$3 million University Endowed Chairs; the Barbara Cox Anthony University Chair in Orthopaedics (held by Dr. Laurie Goodrich); Iron Rose Ranch Chair (held by Dr. Chris Kawcak); and the Abigail K. Kawānanakoa Chair in Alternative Medicine (supporting Dr. Kevin Haussler). We also have a \$1.5 million Chair in Musculoskeletal Imaging from the estate of Kenneth and Virginia Atkinson and, most recently, a \$6 million Presidential Endowed Chair from John and Leslie Malone named the Leslie Malone Presidential Chair in Equine Sports Medicine that Dr. Mindy Story now holds. Dr. Story, who completed her Ph.D. on cervical pain and dysfunction in 2021, is an assistant professor in equine sports medicine and rehabilitation. The funding also supports one of our equine sports medicine residencies. We continue to pursue endowed funding to make all our positions permanent.

Equine Ambulatory Sports Medicine and Rehabilitation Service: A new veterinary specialty, the American College of Veterinary Sports Medicine and Rehabilitation, was accredited by the American Veterinary Medical Association May 2009. There were 27 charter diplomates established by a nomination and Delphi election system. Four of our faculty, Drs. C. Wayne McIlwraith, Kevin Haussler, Chris Kawcak, and David Frisbie, were made charter diplomates of the new college. An equine ambulatory sports medicine service was initiated in 2010 from within the ORC, and has now grown to the following members; Drs. Kawcak, Frisbie, Haussler, Melissa King, Mindy Story, Erin Contino, and Katie Seabaugh. There are now four clinical technicians/administrative assistants: Michelle Alexander, Becca Cedar, Meredith Park, and Shelby Roberts assisting in this service offering state-of-the-art expertise in equine ambulatory neuromusculoskeletal problems in athletic horses. The service has three sports medicine residents (one in each year) and has graduated 12 residents from the three-year program in equine sports medicine and rehabilitation. See our program spotlight on page 36.

Unrestricted Funding from Donors and Foundations: We have continued with good support and have been further able to increase faculty and staff positions, despite the COVID-19 pandemic that caused significant shutdowns, delays, and reorganization efforts. Donor support is critical to our continued operation and growth. In 2022, Ms. Gail Holmes donated \$200,000 towards a residency program in equine sports medicine and rehabilitation, allowing the continued support of a resident for 3 years. Our team came through this dark time with dedication and resolve, and has carried on our mission through expanded translational efforts.



DONORS

With grateful acknowledgment to those who are so critical to the continued success of our program

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PHILANTHROPY FUELS INNOVATION

The transformative power of relationships and a shared passion for horses



Chelsea Magness was first introduced to Colorado State University's equine services through referring equine veterinarian, Dr. Lee Mueller. Dr. Mueller was a long-time partner with CSU's equine hospital and had a strong relationship between the equine referral service and his thriving practice for over 20 years. Dr. Laurie Goodrich, Orthopaedic Research Center Director at CSU, and Dr. Lee Mueller worked tirelessly on horses through the years and had many success stories saving horses lives and returning them back to their sports. As Dr. Mueller entered retirement from his very productive career, it was important for him to help support CSU's equine program and the building of their state-of-the-art new equine hospital. His close relationship with the Magness family through the years led to discussions of how they could help as well.

The Gary Magness Family Foundation became an instrumental partner in supporting the construction of the Johnson Family Equine Hospital. The "rounds" room seemed like a perfect fit to proudly display the Magness Family Foundation name because it is within these rooms, both surgery and medicine, where clinicians review cases with the junior and senior students that are rotating through the clinical services. Important clinical concepts are taught to the DVM students, and extensive, productive and intellectual exchanges occur between mentors and mentees over critical cases in these very rooms. Chelsea shared, "we jumped at the opportunity to give back to the equine program!" because over the years Chelsea built many lasting relationships with several veterinarians in the equine program at CSU, including Dr. Laurie Goodrich.

Power of Philanthropy

As a passionate horse lover and philanthropist, Chelsea has spent her life enjoying the profound bond between humans and horses. "Horses have become so much more than just simple livestock," remarks Chelsea, "they have evolved into these extraordinary athletes through their talent, instinct, and dispositions." Chelsea always knew that if one of her or her family's horses had a serious injury or illness, CSU would be there to help. "Having the strength and expertise of CSU's Veterinary Hospital, and the amazing team behind it, was such a comforting safety net growing up," says Chelsea.

Chelsea's support turned personal in 2022, when her 19-year-old beloved show jumper, Candyman, experienced a career-ending suspensory ligament tear. After Candyman's initial examination, Dr. Goodrich thought he may be a suitable candidate for a new procedure, Tenex. "Dr. Goodrich called me immediately when she learned from Dr. Mueller of Candyman's injury. She offered me her expertise, and most of all, hope in giving Candyman a shot at maximizing the often frustrating lack of healing that suspensory ligaments are known for" Chelsea recalled. "She explained the relatively new concept of Tenex, how Candyman could benefit from it, and how it would be a great experience for the hospital as well."

"(HORSES) HAVE EVOLVED INTO THESE EXTRAORDINARY ATHLETES THROUGH THEIR TALENT, INSTINCT, AND DISPOSITIONS"

Road to Recovery

The Tenex procedure is a minimally invasive technique targeted towards treating direct sites of chronic tendon and ligament injury which can be extremely challenging to heal. Similar to the process used to treat cataracts for eye problems, this procedure sonicates and removes damaged tissue within the tendon or ligament to restart the healing process. Despite its apparent value in treating tendon and ligament disease, there is little understanding of this procedure. Notably Dr. Bradley Nelson, Assistant Professor of Equine Surgery & Lameness and a clinician scientist within the ORC, received funding from the Orthopaedic Research Center Philanthropic Funds to more deeply investigate how this technique works in horses. The philanthropic funds that Dr. Nelson originally received, resulted in enough initial data to then be awarded a highly competitive national award from the Grayson Jockey Club Research Foundation to both study and optimize the Tenex procedure effects on tendons and ligaments. Learn more about the importance of philanthropy in research from Dr. Nelson: <https://col.st/xrIHe>.

After recovery from Tenex treatment, Candyman then spent 6 weeks in the Equine Sports Medicine & Rehabilitation program under the guidance of Dr. Melissa King, Professor of Equine Sports Medicine and Rehabilitation. Candyman's rehabilitation consisted of a combination of physical therapy, therapeutic modalities, range of motion exercises, cryotherapy, and controlled exercises incorporating surface variations, proprioceptive exercises, and ground poles. Physical therapy protocols were designed specifically for Candyman's case to decrease pain and inflammation, promote healing, reduce tissue thickening/restriction, enhance neuromotor control, restore muscle strength and improve range of motion.

In addition to therapeutic exercises and core strengthening, several rehabilitation modalities were utilized to target Candyman's injury. Cryotherapy was utilized as a means of reducing inflammation, and laser therapy was used to aid in decreasing inflammation and improve healing of his injuries. Pulsed electromagnetic field therapy was applied to modulate pain and decrease inflammation, while therapeutic ultrasound was used to decrease peri-ligamentous thickening and improve tissue extensibility. Much of the techniques Dr. King uses to rehabilitate horses is derived from cutting edge research she and her team within the ORC have performed for decades.

Following the treatment regimen, an ultrasound examination showed impressive repair of this severe ligament injury. While Candyman did not return to show jumping at the age of 20, he is now able to comfortably travel and is happily enjoying the retired life- ruling the pastures of Elizabeth, Colorado.

Chelsea and the Gary Magness Family Foundation believe strongly that as a community, transformative advancements can be made in the health and welfare of horses through strategic collaborative partnerships. "I was elated to have the opportunity to give 'Candy' a higher quality of life, and to help the hospital further their research with this procedure; all because of the relationship I was able to build with Dr. Goodrich," says Chelsea.



Giving Opportunities

The Orthopaedic Research Center at Colorado State University continues its mission daily to investigate the pathogenesis, diagnosis, treatment, and prevention of musculoskeletal disease and injury for the betterment of both animals and humans. Groundbreaking advancements in orthopaedic treatments are a result of support and partnerships, and the ORC is made better daily by the philanthropic generosity of many over the years. Thank you to all who support, and to all who will in the future.

If you have questions about giving opportunities, please contact Sarah Schmidt, Assistant Vice President of Advancement, at s.schmidt@colostate.edu.



advancing.colostate.edu/ORCE

TRANSLATABLE RESEARCH

CSU veterinarians expand on key equine orthopedic research that could also benefit people

story by Christopher Outcalt
photos by Joe A. Mendoza
Colorado State University



It was early November, and Dr. Lynn Pezzanite was standing in an operating room at Colorado State University's Translational Medicine Institute, flanked on either side by two of her most influential mentors, Dr. Laurie Goodrich and Dr. Jason Stoneback. Goodrich and Stoneback had scrubbed in to assist on a pair of equine surgeries tied to Pezzanite's first research grant as the principal investigator.

"They've been such supporters collectively in my success," Pezzanite said. "It was surreal to be in that position."

Building on findings from her postdoctoral work, Pezzanite, an equine surgeon and an assistant professor in cellular and molecular biology, was embarking on a study designed to better understand how immune cells behave as osteoarthritis progresses in horses. The degenerative joint disease is one of the most common disorders that equine veterinarians encounter, impacting

up to 80% of horses older than 15. Treatment options, however, remain limited.

The idea behind Pezzanite's study — funded by a two-year grant from the nonprofit Grayson-Jockey Club Research Foundation — was that examining the early-stage immune response to osteoarthritis might allow the group to identify certain biological markers of different stages of the disease. From there, the team could perhaps tailor treatments or gene therapies to specific stages, helping prevent the disease's progression. "We're really trying to look at: What is the best timing to intervene?" Pezzanite said.

Stoneback's presence in the operating room signaled another research goal. As the University of Colorado Anschutz Medical Center chief orthopedic trauma surgeon and director of CU's Limb Restoration Program, Stoneback works with humans, not horses. Nevertheless, he views the research being done by Pezzanite, Goodrich — who directs CSU's Orthopaedic Research Center — and others at the Translational Medicine Institute, including Dr. Steven Dow, as potentially "game-changing" for his own practice.

"The work going on here," Stoneback said, "could have direct translational impact in humans."

Some exceptional people

Stoneback is among a small group of physicians worldwide who regularly perform an innovative procedure that involves implanting a metal orthopedic rod into an amputee's residual limb. The method, known as osseointegration or bone-anchored limb replacement, is considered superior to fitting an amputee with a traditional prosthesis because the implant connects directly with the patient's body, helping to improve awareness, balance and gait.



One of Stoneback's most significant challenges is controlling possible infection. The standard methods don't always work well with his patients; for instance, antibiotics won't prevent bacteria living on metal. "The biggest concern we have is that the area gets catastrophically infected and we can't control it," he said, "and then we have to remove the device."

Searching for new ways to approach that problem is what led Stoneback to collaborate with CSU's Translational Medicine Institute. First established in 2018, the partnership has resulted in multiple projects aimed at developing innovative approaches to treat infection and other complications that occur after trauma, including the osteoarthritis work launched in November.

A world-class human surgeon, Stoneback had been looking forward to the experience in the equine operating room. "Instead of being the person who people are looking to for guidance and directing exactly what's going to happen, I'm here as an observer and a participant," he said. "It's super cool to come and learn from such exceptional people."

During surgery, the team worked to create a tiny chip in the horse's cartilage. The procedure is designed to induce a small amount of inflammation in the joint, prompting an immune response. During the next four months, Pezzanite would then monitor and study what happened. "I'll take tissue samples and look at how the gene expression changes at a single cell level," Pezzanite said. "Hopefully that will inform us further on biomarkers of disease progression and the best timing to intervene."

Top choice

Pezzanite attended vet school in upstate New York at Cornell University. Her mother was a veterinarian, and Pezzanite always had a sense that she would spend her career working with horses too. When it came time to apply for residency, Pezzanite was attracted to CSU because of the University's strong reputation as a hub for orthopedic research. "This was my top choice," Pezzanite said. "I really only wanted to come here."

After residency, Pezzanite remained at CSU to work on her postdoctoral degree. She dug further into the intersection of orthopedic research and immunology, collaborating with Goodrich and Dow, director of CSU's Immunotherapy Research Laboratory housed within the Translational Medicine Institute and Flint Animal Cancer Center.

Working in vitro as well as in rodent models, Dow had pioneered immunotherapies designed to treat antimicrobial-resistant infection. That work presented an opportunity for Pezzanite: Testing the effectiveness of Dow's therapies in horses became the foundation of her postdoc research. "I was starting my Ph.D.," Pezzanite said, "and we were interested in taking this forward in a larger animal model."

Around the same time, Dow met CU's Stoneback at a conference in Denver. When Stoneback learned about Dow's immunotherapy research an idea clicked: He thought the immune-activated cellular therapies might help with the infection challenges he sees with his patients and expressed interest in integrating the work into his limb restoration practice. From there, a wider partnership formed. Stoneback joined Pezzanite's postdoctoral committee, and she regularly traveled to Denver to shadow Stoneback in his operating room and learn from his practice.

In October 2022, Pezzanite, Dow and Goodrich published promising results from the horse therapy trials in the journal *Annals of Translational Medicine*. After that, Pezzanite began to think through next steps, both for the research and for her career. She had multiple offers to join faculty at other schools but decided to stay in Fort Collins in no small part because of the support from Dow, Goodrich and Stoneback. "All three of them have been instrumental in me staying," she said.



The experience with Stoneback's practice in particular made Pezzanite realize that she wanted to focus specifically on translational medicine, researching therapies that would benefit animals but that could also be applied to advancements in human medicine.

"I initially viewed the potential for our work to help people as an added benefit," Pezzanite said. "And now, I honestly view work that benefits both animals and people as our primary focus."

A well-positioned leader

Within the past 10 years, Goodrich said, the concept of translational medicine has become more widely accepted and practiced in the broader scientific research community. What's more, Goodrich believes that CSU's Translational Medicine Institute is well positioned to be a leader in the growing field. "Right now, across the country and the world, you're seeing a lot of translational medicine centers pop up," Goodrich said. "But very few of them are at veterinary institutions."

Having the institute situated at a university with so many veterinarians who are both skilled researchers and clinicians is a huge asset, Goodrich said. "Clinician scientists are the ones who take these therapies and use them with their patients," she said. "It's very translational because they can go back and forth between clinics and the lab environment to investigate."

Pezzanite, Goodrich said, is an excellent example of exactly that kind of translation scientist. "She's been outstanding in every part of her training here," Goodrich said. "She has an amazing capacity to take an idea and turn it into a grant and execute the work — and she's a great mentor to her students as well."

For her part, Pezzanite plans to have some initial results from her research grant sometime this summer. From there, she hopes to expand her work, both building on the osteoarthritis study and pursuing other ways to treat infections in patients with orthopedic implants. "Musculoskeletal, particularly joint-related, disease is a major focus for my program moving forward," she said. "We look forward to continued collaborations with Dr. Stoneback and his team aimed at improving outcomes in post-traumatic orthopedic conditions. The goal is to eventually run a clinical trial in humans."

Even then, Pezzanite might still be reflecting on how much that day in the operating room with Goodrich and Stoneback meant to her and her career.



Awards and Recognition

Dr. Charlie Barton – 1. 1st Place, Outstanding Surgery Resident Clinical Presentation Award, American College of Veterinary Surgeons. 2. J.E. Bruemmer-Horwitz Graduate Equine Research Fellowship Award

Dr. Laurie Goodrich – Honored Mentor Award, American College of Veterinary Surgeons

Dr. Brad Nelson – Outstanding Author, Annals of Translational Medicine Journal

Dr. Lynn Pezzanite – 1. Zoetis Award for Veterinary Research Excellence. 2. Wiley Top Cited Author (5 manuscripts)

Dr. Lauren Smanik – Bloomberg Award for Best Clinical Research Abstract

Dr. Zoe Williams – T32 Postdoctoral Fellowship Program, National Institutes of Health (NIH)



Dr. Charlie Barton Awarded American College of Veterinary Surgeons' Outstanding Resident Award

The Orthopaedic Research Center would like to congratulate Dr. Charlotte (Charlie) Barton, BVetMed, MRCVS, for her 2023 American College of Veterinary Surgeons (ACVS) Outstanding Surgery Resident Award. Dr. Barton received the first-place award in the category Large Animal Residents' Forum Presentation: Clinical for her work titled "Fasting Horses Perioperatively Decreases Manure Production and Increases Time to Output Postoperatively."

According to the ACVS website, the Outstanding Surgery Residents' Awards competition was established to "encourage the development of clinically important research and the dissemination of the results of these investigations, particularly those conducted by surgery residents." Awards are presented in the following categories: Large Animal Residents' Forum

Presentation (Research and Clinical), Small Animal Residents' Forum Presentation (Research and Clinical), Veterinary Surgery Publication, and Poster Presentation. The Presentations, publications, and posters must represent the original work of the resident, and the residents' studies may be prospective or retrospective clinical studies, or controlled laboratory research.

Dr. Barton's novel research is exciting and pivotal to equine health. "I am engaged in research relevant to how we manage orthopedic elective surgical cases pre- and post-operatively," says Dr. Barton. "This research evaluates three perioperative feeding protocols on postoperative manure and colic incidence. This study has changed the standards of feeding horses before and after general anesthesia for elective cases both throughout equine clinical and research programs." Dr. Barton's findings identified a significantly reduced risk of post-anesthetic complications, such as a lack of manure production and colic in horses that did not have feed withheld. Additionally horses had improved well-being by not having to wear a muzzle and have hay withheld for an extended period of time.

Photo, left to right: Dr. Rachel Hector, Dr. Charlie Barton, Dr. Laurie Goodrich at the 2023 ACVS award ceremony.

To learn more about this research, check out the JAVMA/AJVR "Veterinary Vertex" podcast episode featuring Drs. Charlie Barton and Rachel Hector:



<https://col.st/TtlmZ>

CLINICAL TRIALS

About Clinical Trials

Clinical trials are research studies that help medical professionals improve the detection and treatment of illnesses. Our clinical trials program enrolls client-owned horses to evaluate the effectiveness of new drugs such as blood-derived biologics, mesenchymal stem cells therapies, and gene therapy techniques to treat orthopedic diseases. Many of the musculoskeletal treatments used in horses today are the result of pre-clinical trials within the Orthopaedic Research Center, specifically the use of corticosteroids and novel biologic therapies. We learn valuable information from every patient, and we use this information to improve their care as well as the care of future patients, both horses and people.

Each clinical trial has specific eligibility criteria that need to be fulfilled for a horse to participate, and these vary among studies. Some clinical trials are designed for horses with a particular diagnosis of orthopedic disease (i.e. osteoarthritis), while others are open to horses with a variety of orthopedic abnormalities. In general, to qualify for Colorado State University's trials, horses need to have a specific musculoskeletal problem that is diagnosed by their veterinarian or one of veterinarians, and are otherwise healthy. Owners also must be willing to comply with study protocols and commit to coming into the clinic for the visits that are required by the trial.

Why are Clinical Trials Important

With help from equine participants, clinical trials help doctors in the medical and veterinary fields discover disease prevention methods and find new ways to improve detection, diagnosis, and treatment of animal illnesses, all while enhancing the quality of care each patient receives. The clinical trials within the ORC contribute to research that discovers better treatments for horses and people with orthopedic disease, and provide an alternative when standard treatment options are no longer effective. Our clinical trials also explore new therapies to treat disease that is unlikely to have a significant response to standard treatment. Finally, clinical trials offer financial assistance for potentially life-saving treatments that clients otherwise may not be able to afford.

Prostride Clinical Trial

Dr. Erin Contino and Dr. Laurie Goodrich

Sponsored by: Zoetis

"Evaluation of autologous protein solution (Prostride) as an intra-articular anti-inflammatory therapy for adult horses."

This double blinded clinical trial is currently enrolling horses with naturally occurring lameness of the stifle (specifically the medial femorotibial joint). Horses will be randomly divided into two groups and treated with either Prostride or corticosteroid/hyaluronan and followed over 6 months to assess response to treatment.

For more information on study protocols, eligibility, and owner responsibilities please visit:



JMV Digital

 <https://col.st/v2oii>

eQcell, Inc Clinical Trial

Dr. Katie Seabaugh and Dr. Laurie Goodrich

This trial is completed, findings are forthcoming.

Sponsored by: eQcell, Inc.

"Evaluation of allogeneic umbilical cord blood-derived mesenchymal stromal cells for treatment of synovitis in horses."

The purpose of this study is to evaluate the efficacy and dosing of a single administration of frozen allogeneic mesenchymal cells at a dose of either 10 million activated (stimulated) umbilical derived mesenchymal stromal cells or 10 million nonactivated (unstimulated) umbilical derived mesenchymal stromal cells for the treatment of synovitis. Horses are randomly assigned to one of two groups. This ongoing clinical trial is assessing naturally occurring lameness isolated to one carpal joint, or front or hind fetlock.

For more information on study protocols, eligibility, and owner responsibilities please visit:



 <https://col.st/39Afj>

Freeze-Dried Conditioned Serum Clinical Trial

Dr. Erin Contino and Dr. David Frisbie

"Evaluation of the safety and efficacy of intra-articular allogeneic freeze-dried conditioned serum (FDCS) in horses with lameness regionalized to the distal interphalangeal joints."

This clinical trial will be starting soon and aims to compare freeze dried allogeneic conditioned serum (conditioned serum is also referred to as IRAP) to a placebo treatment. Horses with naturally occurring lameness isolated to the front feet will be eligible for enrollment.

For more information on study protocols, eligibility, and owner responsibilities please visit:

 <https://col.st/ac7tJ>





FOCUS 1

Promote the Repair and Optimal Health of Neuro-Musculoskeletal Tissues

- a. Orthobiologic therapies
- b. Pharmacologics
- c. Surgical techniques
- d. Physiotherapy, rehabilitation, and conditioning

Publications and Presentations

Textbook Chapters

Dow S, Pezzanite L, Chow L. Immunotherapy options for managing chronic infectious diseases. *Small Animal CVT*. In press.

Haussler K. Functional anatomy and biomechanics of the axial skeleton. *Essential Facts of Equine Physical Therapy, Rehabilitation and Sports Medicine*. In press.

Haussler K. Chiropractic. *Essential Facts of Equine Physical Therapy, Rehabilitation and Sports Medicine*. In press.

King M. Aquatic therapy. *Essential Facts of Equine Physical Therapy, Rehabilitation and Sports Medicine*. VBS GmbH.

King M, Clayton H. Active therapeutic exercises. *Essential Facts of Equine Physical Therapy, Rehabilitation and Sports Medicine*. In press.

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Pezzanite L, Chow L, Dow S, Goodrich L, Schnabel L, Gilbertie J. Antimicrobial properties of equine platelets and stem cells and future horizons. *Veterinary Clinics of North America: Equine Practice*. 39: 565-578.

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Spriet M, Vaughan B, Barrett M, Galuppo L. Advances in regional vascular injection techniques for the delivery of stem cells to musculoskeletal injury sites. *Veterinary Clinics: Equine Practice*. 39: 503-514.

Refereed Publications

Afzali M, Pannone S, Martinez R, Campbell M, Sanford J, Pezzanite L, Kurihara J, Johnson V, Dow S, Santangelo K. Intravenous injection of adipose-derived mesenchymal stromal cells benefits gait and inflammation in a spontaneous osteoarthritis model. *Journal of Orthopedic Research* 2023 April; 41(4):902-912. PMID: 36030381.

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Ammons D, Chow L, Larson B, Goodrich L, Dow S, Pezzanite L. Transcriptomic response in osteoarthritis using single-cell RNA sequencing approaches in an equine model. University of Colorado 5th Annual Orthopedic Research Symposium & D'Ambrosia Diversity Lectureship. Denver, CO. Poster.

Boxleitner T, Pezzanite L, Thampi P, Dow S, Chow L, Goodrich L, Johnstone B. Immunomodulatory effects of articular chondroprogenitor cells. AAVMC Veterinary Scholars Symposium. Puerto Rico. Poster.

Boxleitner T, Pezzanite L, Thampi P, Dow S, Chow L, Goodrich L, Johnstone B. Immunomodulatory effects of articular chondroprogenitor cells. University of Colorado 5th Annual Orthopedic Research Symposium & D'Ambrosia Diversity Lectureship. Denver, CO. Poster.

Colla S, Johnson J, McGilvray K, Zanotto G, Seabaugh K. Biomechanical Assessment of the Collateral Ligament of the Distal Interphalangeal Joint of the Horse following Alterations to the Palmar Angle. American College of Veterinary Sports Medicine and Rehabilitation Annual Conference, Charleston, SC.

Goodrich L. a. Fetlock Internal Fixation and Distal Interphalangeal Joints Laboratory; b. Carpal Slab Fracture, Internal Fixation, and Carpal Sheath Wet Laboratory; c. Navicular Bursoscopy. Colorado State University, Continuing Education Advanced Short Course. Fort Collins, CO.

Goodrich L. a. Arthroscopic Surgery of the Carpus Laboratory; b. Arthroscopic Surgery of the Tarsocrural Joint Laboratory; c. Arthroscopic Surgery of the Fetlock Joint Laboratory; d. Proximal Hind Limb– Stifle and Hock Wet Laboratory; e. Distal Limb Wet Laboratory; f. Basic Arthroscopic Techniques and Diagnostic Arthroscopy. Colorado State University, Continuing Education Short Course. Fort Collins, CO.

Goodrich L. a. Postoperative Management of Osteochondral Repair; b. Subchondral Bone Cyst Management; c. SBC Screw Placement Laboratory; d. Third Carpal Bone Laboratory; e. PSB Fracture Repair Laboratory; f. MC Condylar Fracture Repair Laboratory. Colorado State University, AO North America Advanced Course. Fort Collins, CO.

Goodrich L. a. Management of Orthopedic Infection; b. Surgical Approach and Plate Application of Simple Olecranon Fractures, AO North America Principles in Equine Fracture Course. Columbus, OH.

Haussler K. a. Biomechanical effects of HVLA thrusts: Literature review; b. Neurological effects of HVLA thrusts: Literature review; c. Practical training– Manipulation vs. Mobilization vs. Activator; d. Equine chiropractic research: Literature review; e. Treatment of neck pain and dysfunction. The Art & Science of Spinal Manipulation Therapy for The Advanced Practitioner, Applied Biomechanics and Rehabilitation Academy (ABnR), Lüsche, Germany.

Haussler K. Athletic conditioning: From A to Z in less than 30 seconds. Healing Oasis Wellness Center's Annual Conference. National University of Health Sciences, Lombard, IL.

Haussler K. Cervical articular process morphology: Clinical effects in horses. First Annual Conference of the American College of Veterinary Sports Medicine and Rehabilitation, Charleston, SC.

Kim L, Kreitner K, Scott D, Seabaugh K, Duncan C, Magzamen S. BREATHE: Understanding the relationship between air pollution and horse racing performance in California. COHA CCTSI, Washington, D.C. Poster.

King M. EMF, PEMF, Bio-electromagnetic energy regulation: Does it work? American College of Veterinary Sports Medicine and Rehabilitation Symposium. Charlotte, NC.

King M. Rehabilitation Approaches for Equine Stifle Dysfunction. The International Society of Equine Locomotion. Glendale, AZ.

King M. a. Equine Aquatic Therapy – Scientific review and clinical applications; b. Equine Axial Skeleton Dysfunction and Rehabilitation. Centaur Biomechanics. Virtual Lecture.

King M. Scientific Review of PEMF Therapies. Online Pet Health. Virtual Lecture.

Larson B, Ammons D, Chow L, Goodrich L, Dow S, Pezzanite L. Synovial transcriptomic response in osteoarthritis progression determined by single cell sequencing in an equine model. CSU CVMBS Day, Fort Collins, CO. Poster.

Luque R, Koch T, Goodrich LR, Giraldo A, Valverde A, Zur Linden A, Beehler Marfisi J, Koenig J. Mesenchymal stromal cells for the treatment of surgically induced equine fetlock osteoarthritis. ECVS. Krakow, Poland.

Luque R, Koch T, Goodrich LR, Giraldo A, Valverde A, Zur Linden A, Beehler Marfisi J, Koenig J. Mesenchymal stromal cells for the treatment of surgically induced equine fetlock osteoarthritis. American College Veterinary Sports Medicine and Rehabilitation Symposium. Charleston, NC.

Marshall-Gibson M, Durham M, Seabaugh K, Moorman V, Ferris D. Survey of equine veterinarians regarding primary equine back pain in the United States. American College of Veterinary Sports Medicine and Rehabilitation Annual Conference, Charleston, SC.
Maldonado M, Parkinson S, Story, M, Haussler K. Chiropractic treatment of lameness and concurrent axial skeleton pain and dysfunction in horses. International Conference on Equine Locomotion 9 (ICEL9), Utrecht, The Netherlands. Comparative Exercise Physiology; 19 (Suppl 1): S35.

Montoya T, Buntin B, D'Amato M, Graham K, Williams S, Ward T, Bisazza K, Easley J, Sikes K. Design and Implementation of A Static Weight Bearing Device For Use In Ovine (Sheep) Preclinical Studies. Rocky Mountain Bioengineering Symposium. Fort Collins, CO. [Mentee Award: Second Place, Oral Presentation]

Moorman V, Piquini G, Bass L, Pezzanite L. Initiation of training on lameness and hoof morphology and symmetry in two and three-year-old Quarter Horses. ACVMSR Symposium, Charleston, SC. Poster.

Nelson B. Arthroscopy & Arthroscopic Assisted Fracture Repair. American College of Veterinary Surgeons Large Animal Residents Workshop Webinar Orthopedics. Virtual.

Nelson B. Pedicle screw and rod fixation as a technique for ventral cervical stabilization in horses. Equine Spine Initiative, Lexington, KY.

Nelson B. Navicular Bursoscopy: A Review and Current Evidence. American College of Veterinary Surgeons Surgical Summit. Louisville, KY.

Nout-Lomas Y. Management of seizures. Panel. IVECCS, Aurora CO.

Patel A, Piquini G, Chow L, Impastato R, Hendrickson D, Dow S, Pezzanite L. Transcriptomic responses in horses with progressive osteoarthritis. AAVMC Veterinary Scholars Symposium. Puerto Rico. Poster.

Patterson H, Yocom A, Seabaugh K, Kawcak C and Contino E. The effect of various perineural analgesia techniques of interleukin-1b-induced synovitis of the equine metacarpophalangeal joint. Proceedings 69th Annual Convention American Association of Equine Practitioners.

Patterson H, Yocom A, Seabaugh K, Kawcak C and Contino E. The effect of various perineural analgesia techniques of interleukin-1b-induced synovitis of the equine metacarpophalangeal joint. Poster: 1st annual ACVMSR Symposium.

Pezzanite L, Chow L, Griffenhagen G, Bass L, Goodrich L, Impastato R, Dow A. Distinct differences in immunological properties of equine orthobiologics revealed by functional and transcriptomic analysis using an activated macrophage readout system. ACVMSR Symposium, Charleston, SC. Poster.

Pezzanite L. Joint therapies: Updates on mesenchymal stromal cells and extracellular vesicles. American College of Veterinary Surgeons (ACVS), Louisville, KY.

Pezzanite L, Chow L, Griffenhagen G, Bass L, Goodrich L, Impastato R, Dow S. Functional differences in orthobiologics. American College of Veterinary Surgeons (ACVS), Louisville, KY.

Pezzanite L, Hendrickson D. Updates on wound care – biofilms and wound dressings. Northeast Association of Equine Practitioners (NAEP), Saratoga, NY.

Pezzanite L, Schnabel L. Updates on orthobiologic therapies in equine practice. Northeast Association of Equine Practitioners (NAEP), Saratoga, NY.

Plaisance C, Chow L, Engiles J, Goodrich L, Dow S, Pezzanite L. Transcriptomic response of equine synovial tissues following immune conditioned cellular therapy to treat septic arthritis. Annual Biomedical Research Conference for Minoritized Scientists (ABRCMS), Phoenix, AZ. Poster.

Pezzanite L. Navicular bursoscopy: indications and outcomes. Northeast Association of Equine Practitioners (NAEP), Saratoga, NY.

Pezzanite L, Dow S. Updates on intra-articular antibiotic and local anaesthetic use in equine practice. Northeast Association of Equine Practitioners (NAEP), Saratoga, NY.

Pezzanite L, Ammons D, Chow L, Goodrich L, Dow S. Transcriptomic response to osteoarthritis. American College of Veterinary Surgeons (ACVS), Louisville, KY. Poster.

Pezzanite L, Timkovich A, Sikes KJ, Chow L, Hendrickson D, Becker J, Webster M, Santangelo K, Dow S. Erythrocyte removal from bone marrow aspirate concentrate improves efficacy as intra-articular cellular therapy in a rodent osteoarthritis model. Orthopedic Research Society, Dallas, TX. Poster.

Pezzanite L, Chow L, Phillips J, Griffenhagen G, Moore AR, Schær T, Engiles J, Werpy N, Gilbertie J, Schnabel L, Antczak D, Miller D, Dow S, Goodrich L. TLR-activated mesenchymal stromal cell therapy and antibiotics to treat multi-drug resistant Staphylococcal septic arthritis in an equine model. University of Colorado 5th Annual Orthopedic Research Symposium & D'Ambrosia Diversity Lectureship. Denver, CO. Poster.

Rockow M, Chow L, Impastato R, Webster A, Hendrickson D, Santangelo K, Dow S, Pezzanite L. Immune activated MSC for treatment of osteoarthritis in mouse models. AAVMC Veterinary Scholars Symposium. Puerto Rico. Poster.

Rockow M, Chow L, Impastato R, Hendrickson D, Santangelo K, Dow S, Pezzanite L. Immune activated cellular therapy for treatment of osteoarthritis. University of Colorado 5th Annual Orthopedic Research Symposium & D'Ambrosia Diversity Lectureship. Denver, CO. Poster.

Rockow M, Chow L, Impastato R, Webster M, Hendrickson D, Santangelo K, Dow S, Pezzanite L. TLR-3 priming of mesenchymal stromal cells (MSC) improved cellular treatment of osteoarthritis in a murine model. CSU CVMBS Day, Fort Collins, CO. Poster.

Schnabel L, Pezzanite L. Antimicrobial properties of equine stromal cells and platelets. American College of Veterinary Surgeons (ACVS), Louisville, KY.

Silliman B, Montoya T, Batson S, Winston S, Pezzanite L, McGilvray K, Easley J, Sikes K. Development of a surgical model for rotator cuff tendon degeneration in the rat. AAVMC Veterinary Scholars Symposium. Puerto Rico. Poster.

Smanik L, Selberg K, Kawcak C, Stewart H, Goodrich L. Computed tomography and fluoroscopy versus radiographic guidance for internal fixation of simulated dorsomedial-plantarolateral central tarsal bone fractures in non-racehorses. Veterinary Orthopaedic Society Conference. Big Sky, Montana.

Story M. Medical and surgical treatments for cervical pain and dysfunction. American College of Veterinary Surgeons. Lexington, KY.

Thampi P, Seabaugh K, Pezzanite L, Phillips J, Grieger J, McIlwraith CW, Chu C, Samulski R, Goodrich L. Optimization of scAAVIL-1ra dose in a large animal model of post-traumatic osteoarthritis. Orthopedic Research Society, Dallas, TX. Poster.

Thampi P, Samulski J, Grieger J, Phillips J, McIlwraith CW, Goodrich L. Characterization of scaavil-1ra/igf-1 combination gene therapy in equine chondrocytes and synoviocytes. Orthopedic Research Society Annual Meeting, Dallas, TX. Poster.

Winston S, Pezzanite L, Impastato R, Sikes K, Santangelo K, Dow S, McGilvray K. Immune instructive printed scaffolds to stimulate healing in rotator cuff tendon injury. University of Colorado 5th Annual Orthopedic Research Symposium & D'Ambrosia Diversity Lectureship. Denver, CO.



FOCUS 2

Investigations of the Origins of Neuro-Musculoskeletal Disease

- a. Neuro-musculoskeletal pain and dysfunction
- b. Biomechanics and sensory input
- c. Repetitive stress response
- d. Cell markers

Publications and Presentations

Textbook Chapters

Dow S, Pezzanite L, Chow L. Immunotherapy options for managing chronic infectious diseases. *Small Animal CVT*. In press.

Rawlinson JE, Pezzanite L, Griffenhagen G. Local anesthesia of the equine head and neck. *Large Animal Local Anesthesia*. Wiley Publishing. In press.

Refereed Publications

Brock B, Greer H, Honnas C, Gilleland B, Barrett M, Moore J, Cohen N. A randomized, self-controlled case series evaluating core osteostixis of osseous cyst-like lesions of the navicular bone to improve lameness in horses with podotrochlear syndrome. *Veterinary Medicine (Auckland)* 2023 March; 14:35-46. PMID: 36945679.

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Johnson S, Sikes K, Thampi P, McConnell A, Coghlan R, Johnstone B, Santangelo K, Frisbie D. Fast, non-eccentrically loaded exercise worsens tendinopathic healing responses in a murine model. *American Journal of Veterinary Research* 2023 April; 84(6). PMID: 37044374.

Johnson J, Von Stade D, Gadowski B, Regan D, Easley J, Sikes K, Troyer K, Tianjian Z, Schlegal T, McGilvray K. Biomechanical and Histological Changes Secondary to Aging In The Human Rotator Cuff: A Preliminary Analysis. *Journal of Orthopaedic Research* 2023 October; 41(10):2221-2231. Epub February; . PMID 36722700.

Kawahisa-Piquini G, Bass L, Pezzanite L, Moorman V. Effect of age at training initiation on hoof morphology and lameness in juvenile American Quarter Horses. *Equine Veterinary Journal* 2023 September; 55(5):765-776. Epub January. PMID: 36572927.

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Marshall-Gibson M, Durham M, Seabaugh K, Moorman V, Ferris D. Survey of equine veterinarians regarding primary equine back pain in the United States. *Frontiers Veterinary Science* 2023 July; 10:1224605. PMID: 37565081.

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Timkovich A, Sikes K, Andrie K, Afzali M, Sanford J, Fernandez K, Burnett D, Hurley E, Daniel T, Serkova N, Donahue T, Santangelo K. Full and Partial Mid-substance ACL Rupture Using Mechanical Tibial Displacement in Male and Female Mice. *Annals of Biomedical Engineering* 2023 March; 51(3):579-593. PMID: 36070048.

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Research Abstracts, Presentations, Proceedings

Bus R, Nelson B. Optimizing an in vitro model of equine articular cartilage degeneration. *CVMBs Veterinary Summer Scholars program Science Slam.* Fort Collins, CO.

Bus R, Nelson B. Optimizing an in vitro model of equine articular cartilage degeneration. *National Veterinary Summer Scholars Symposium.* San Juan, Puerto Rico.

Gadomski B, Labus K, Johnson J, Nelson B, Puttlitz C, Goodrich L. Biomechanical Comparison of Fresh and Cryopreserved Human Osteochondral Allografts. *International Cartilage Repair Society Scientific Meeting.* Sitges, Spain. Poster.

Haussler K. Asymmetry in Sport Horses: Defining Laterality. Is it laterality or just asymmetry? *First Annual Equine Laterality Workshop, International Taskforce on Laterality in Sport Horses, Utrecht, The Netherlands.*

Kassel B, Montoya T, Easley J, Santangelo K, Sikes K. Age and Sex-related Effects on Myotendinous Junction Injury In Rats. *Orthopaedic Research Society.* Dallas, TX.

Lu A, Sikes K, Guo P, Huard M, Santangelo K, Tashman S, Narkar V, Huard J. Skeletal Muscle Atrophy After ACL Rupture Can Be Mitigated by ERK Overexpression in Skeletal Muscle. *Orthopaedic Research Society.* Dallas, TX.

Michalko B, Sikes K, Brekhus C, Johnson J, Easley J, Nelson B. Biomechanics of the LDE and ACL in ovine stifle stability for a novel model of posttraumatic osteoarthritis. *CVMBs Research Day, Fort Collins, CO.*

Nelson B. Pursuit of a Chronic Tendinopathy Model in the Horse: A more representative way to investigate tendon therapies? *TMI Research in Progress Seminar (RIPS) series.* Fort Collins, CO. July 5.

Potter A, Van Zeeland E, Burton L, Easley J, Nordgren T, Sikes K. Characterization of the FAT-1 Mouse Strain in a Non-Surgical Model of ACL Rupture. *University of Colorado Anschutz Medical Campus Orthopaedic Research Symposium.* Denver, CO.

Rodriguez N, Santangelo B, Sikes K, Santangelo K. Development of a Custom System to Induce Mechanical ACL Rupture In Guinea Pigs. *Rocky Mountain Bioengineering Symposium.* Fort Collins, CO.

Sikes K, Johnson J, Michalko B, Brekhus C, Montoya T, Easley J, Nelson B. Biomechanical Contributions of The LDE And ACL In The Ovine Stifle: Implications For A Novel Model Of Post-traumatic Osteoarthritis. *Orthopaedic Research Society.* Dallas, TX. Poster.

Van Zeeland E, Montoya T, Burton L, Saviola S, Santangelo K, Easley J, Sikes K. Sex-Specific Anterior Cruciate Ligament Proteomes Following Non-Surgical Rupture. *University of Colorado Anschutz Medical Campus Orthopaedic Research Symposium.* Denver, CO.

Van Zeeland E, Kassel B, Wist S, Easley J, Santangelo K, Sikes K. Elucidating Sex Differences in The Response to Anterior Cruciate Ligament Injury Following Mechanical Ligament Rupture. *Orthopaedic Research Society.* Dallas, TX. [Mentee Award: Second Place, Poster Presentation]

Van Zeeland E, Kassel B, Montoya T, Santangelo K, Easley J, Sikes K. Sex differences in the response to anterior cruciate ligament injury following mechanical rupture in a mouse model. *CVMBs Research Day, Fort Collins, CO.* [Mentee Award: First Place, Early Career, Oral Presentation, Translational]





FOCUS 3

Improve the Detection of Neuro-Musculoskeletal Disease

- a. Advanced analytics
- b. Imaging modalities
- c. Interpretation of clinical examination
- d. Novel diagnostic techniques
- e. Behavior

Publications and Presentations

Textbook Chapters

Nelson B, Goodrich L. Elbow and shoulder. Hinchcliff, Kaneps, and Goer, *Equine Sports Medicine and Surgery*, 3rd edition. Saunders Elsevier. Accepted.

Refereed Publications

Acutt E, Zhou T, Mama K, Nelson B, Selberg K, Barrett M. Contrast administration via ultrasound-guided injection of the cranial tibial artery results in contrast enhancement of the soft tissues of the metatarsus in horses undergoing CT. *Veterinary Radiology: Ultrasound* 2023 September; 64(5):904-912. Epub July. PMID: 37406620.

Barrett M, Gorchenko G, Frisbie D. Comparison of Ultrasound and Magnetic Resonance Imaging for Identifying Soft Tissue Abnormalities in the Palmar Aspect of the Equine Digit. *Animals (Basel)* 2023 July; 13(14):2328. PMID: 37508105.

Barton C, Goodrich L. The use of radiofrequency in equine orthopedic surgery. *Journal of American Veterinary Medicine Association* 2023 April; 261(8):1208-1215. PMID: 37116880.

Barton C, Hughes K, Cowan C, Nout-Lomas Y, Nelson B. An Unusual Cause of Femoral Nerve Paresis in a Horse: Disseminated B Cell Lymphoma With Plasmacytoid Differentiation and Direct Neuronal Invasion. *Journal of Equine Veterinary Science* 2023 July; 126:104502. Epub April. PMID: 37120116.

Bisazza K, Nelson B, Sikes K, Nakamura L, Easley J. Computed Tomography Provides Improved Quantification of Trabecular Lumbar Spine Bone Loss Compared to Dual-Energy X-Ray Absorptiometry in Ovariectomized Sheep. *Journal of Bone and Mineral Research Plus* 2023 August; 7(12):e10807. PMID: 38130759.

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Ellis K, Contino E, Nout-Lomas Y. Poor performance in the horse: diagnosing the non-orthopedic causes. *Equine Veterinary Education* 2023 March; 35(4): 208-224.

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Luedke L, Mohammed H, Ducharme N. Decreasing polymethyl methacrylate bone cement concentration extends working and setting times in vitro. *American Journal of Veterinary Research* 2023 September; 84(12). PMID: 37739393.

Stewart H, Easley J, Selberg K, Puttlitz C, Nakamura L, Johnson J, Kawcak C. Experimental models of bone marrow lesions in ovine femoral condyles. *Veterinary Surgery* 2023 February; 52(2):284-298. PMID: 36523261.

Stewart H, Siewerdsen J, Selberg K, Bills K, Kawcak C. Cone-beam computed tomography produces images of numerically comparable diagnostic quality for bone and inferior quality for soft tissues compared with fan-beam computed tomography in cadaveric equine metacarpophalangeal joints. *Veterinary Radiology Ultrasound* 2023 November; 64(6):1033-1036. PMID: 37947254.

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Research Abstracts, Presentations, Proceedings

Barton C, Hector R, Hendrickson D, Kawcak C, Nelson B, Goodrich L. Fasting horses perioperatively decreases manure production and increases time to manure output post-operatively. *American College of Veterinary Surgeons Surgical Summit*. Louisville, KY.

Bisazza K, Nelson B, Sikes K, Easley J. Quantitative Computed Tomography Shows Sustained Trabecular Bone Density Compared To Dual X-ray Absorptiometry In A Sheep Model Of Osteoporosis. *Orthopaedic Research Society*. Dallas, TX. Poster.

Contino E, Kawcak C and Dalglish J. The prevalence of lameness in FEI equine athletes and its correlation to performance. *Proceedings 69th Annual Convention American Association of Equine Practitioners*. San Diego, CA.

Crawford L, Moore B, Haussler K, Nout-Lomas Y, Story M, Aboellail T. Molecular investigations of ganglionitis in performance horses with clinical signs of axial skeletal pain. *Annual Meeting of the American College of Veterinary Pathologists*. Chicago, IL.

Esselman A, Johnson S, Contino E. Substantial variability exists in the interpretation of survey radiographs among equine veterinarians. *Proceedings 69th Annual Convention American Association of Equine Practitioners*.

Johnson J, Gadomski B, Labus K, Stewart H, Nelson B, Seim H, Regan D, von Stade D, Kelly C, Horne P, Gall K, Easley J. Novel 3D Printed Lattice Structure Titanium Cages Evaluated In An Ovine Model Of Interbody Fusion. *Orthopaedic Research Society*. Dallas, TX. Poster.

Haussler K. a. Applied functional anatomy of the equine axial skeleton; b. Functional anatomy of the equine skin and fascia; c. Veterinary chiropractic principles, terminology, and biomechanics; d. Examination of the head and cervical spine; e. Pathology of the equine spine and pelvis; f. Examination of the thoracolumbar spine; g. Examination of the sacropelvic and sacrocaudal regions. *Focus on the Equine Spine: Base Course (Part 1)*. Kootwijkbroek, The Netherlands.

Haussler K. a. Functional anatomy review: Head, neck & cranial thoracic regions; b. Functional anatomy review: Trunk and pelvic regions; c. Equine spinal examination review. *Equine Rehabilitation Certificate Program*. College of Veterinary Medicine, University of Tennessee, Knoxville, TN.

Haussler K. a. Practical training—Head and neck techniques; b. Understanding and differentiating pain behaviors in horses. *The Art & Science of Spinal Manipulation Therapy for The Advanced Practitioner, Applied Biomechanics and Rehabilitation Academy (ABnR)*, Lüsche, Germany.

Haussler K. a. Introduction and course objectives; b. Cervical anatomy; c. Cervical biomechanics; d. Cervical pathology; e. Case presentations; f. Physical examination; g. Medical and surgical treatment; h. Cervical rehabilitation. *Equine Neck Pain and Dysfunction*, Equine-Librium College, Plettenberg Bay, South Africa.

Haussler K. a. Functional anatomy and clinical biomechanics of the equine cervical spine; b. Spinal pathology of the cervical and cervicothoracic regions; c. Soft tissue and Joint mobilization of the cervical region and cervicothoracic junction; d. Joint mobilization of the cervical region. *Proceedings of the Equine-Librium College, Symposium on Equine Neck Pain and Dysfunction*. Plettenberg Bay, South Africa.

King M. Down to the Core: An In-Depth Examination of Equine Core Fitness. *Platinum Performance*. Webinar.

King M. Influence of Lameness of Multifidus Muscle, Implications for Back Function. *Online Pet Health*. Virtual Lecture.

King M. Influence of Lameness of Multifidus Muscle, Implications for Back Function. *American College of Veterinary Sports Medicine and Rehabilitation Symposium*. Charlotte, NC.

Luedke L. Tendon Injury in Thoroughbred Racehorses. *Thoroughbred Horsemen's Association Continuing Education Course Series*, Virtual.

Nelson B, Makela J, Lawson T, Patwa, Snyder B, Grinstaff M, McIlwraith CW, Goodrich L, Kawcak C. Cationic CECT Displays Differences in Articular Cartilage Quality in an In Vivo Equine Model. *International Cartilage Repair Society Scientific Meeting*. Sitges, Spain.

Nout-Lomas Y. Neurological examination in Large Animals. *AVMA*, Denver, CO.

Nout-Lomas Y. Equine Neurologic Examination. *Veterinary Spinal Compendium Equine Neck Pain and Dysfunction In-Person Course*. Fort Collins, CO.

Nout-Lomas Y. Neurology Panel Discussion. *84th Annual Colorado State University Conference for Veterinarians*.

Nout-Lomas Y. Diagnosis, Treatment and Management of Equine Neurologic Disorders for the Field Practitioner. *Merck Animal Health Intervet Canada Corp*, Canada.

Nout-Lomas Y. Diagnostic approach to the acutely neurological horse; *IVECCS*, Aurora, CO.



Smanik L, Selberg K, Kawcak C, Stewart H, Goodrich L. Computed tomography and fluoroscopy versus radiographic guidance for internal fixation of simulated dorsomedial-plantarolateral central tarsal bone fractures in non-racehorses. *Veterinary Orthopaedic Society Conference*. Big Sky, Montana.

Solum G, Johnson S, Contino E. Characterization of radiographic lesions in western performance horses with lameness localized to the fetlock joint. *Proceedings 69th Annual Convention American Association of Equine Practitioners*.

Story M. Diagnosing and managing back pain, including surgery. *Facilitator. American Association of Equine Practitioners Annual Convention*. Virtual.

Story M. Diagnosing and managing back pain, including surgery, *Facilitator. American Association of Equine Practitioners Annual Convention*. San Diego, CA.

Story M. Cervical pain in the horse; what we know and do not know. *American College of Veterinary Surgeons*. Lexington, KY.

Story M. Arriving at a diagnosis of primary neck pain. *Locomotion in Practice*. Utrecht University, The Netherlands.

Story M. The role of feed and supplements in joint homeostasis. *Locomotion in Practice*. Utrecht University, The Netherlands.

Story M. Dorsal root ganglionitis and poor performance. *American College of Veterinary Sports Medicine and Rehabilitation Symposium*. Charleston, SC.

Story M. Lumbosacral pelvic kinematics: diagnosis, treatment and rehabilitation. *Centaur Biomechanics*. Virtual.



EQUINE SPORTS MEDICINE & REHABILITATION

Equine Sports Medicine and Rehabilitation (ESMR) has been a key component and pillar of research since the inception of the Orthopaedic Research Center (ORC) four decades ago. Objective gait analysis, advancing diagnostic methods, use of biologic therapies, evidence based support for various rehabilitation techniques and modalities, acupuncture, and many other therapeutics have all been studied and applied as essential tools to both research and clinical practice. The diagnosis, management and rehabilitation of musculoskeletal pain and dysfunction in the horse is largely informed by the advances in this field, giving us novel methods to both identify early signs for prevention and monitor healing over time.

The ESMR clinical service, as well as the residency program, within the ORC was officially formed in conjunction with the accreditation of the American College of Veterinary Sports Medicine and Rehabilitation (ACVSMR) from the American Veterinary Medical Association in 2009. Colorado State University and the ORC had a major role in developing ACVSMR, with four of the founding members being ORC equine veterinary professors, Drs. Dave Frisbie, Kevin Haussler, Chris Kawcak, and C. Wayne McIlwraith. At the time, equine sports medicine, specifically physical therapy and rehabilitation, was an underserved area of scientific research in veterinary medicine. The specialty service, initiated by Dr. Kawcak, has currently expanded to encompass Drs. Erin Contino, Melissa King, Katie Seabaugh, and Melinda Story, all of whom completed

DVM, MS, PhD, and/or residencies with the ORC. This service has both a clinical mission, that aligns with the CSU Veterinary Health System (VHS) and the Johnson Family Equine Hospital (JFEH), as well as a research mission, supported by the ORC.

CSU is one of only three universities in the United States with an in-house equine rehabilitation center and the only veterinary teaching hospital to have a specialty spine center. The Equine Spine Center allows a complete health system to see patients through their healing journey without having to leave campus, starting with global functional assessments, onto advanced, state of the art diagnostic imaging, surgery, and rehabilitation. ESMR and the ORC also have the unique distinction of having eight board-certified rehabilitation specialist veterinarians. In addition to the founding members, Drs. Erin Contino, Melissa King, Katie Seabaugh, and Melinda Story are all diplomates of the American College of Sports Medicine and Rehabilitation (ACVSMR). These specialists are not only training the next generation of equine focused clinicians, but also guiding them in research techniques that will be important to musculoskeletal research efforts within the ORC program. The ESMR program had the first three ACVSMR residents in the world and have added at least one per year since. There are currently four residents, all of whom are concurrently working towards their Masters degrees. All of the residencies since integration in 2009 have been funded by philanthropic dollars.



JMV Digital

A significant amount of foundational research is occurring to validate therapeutics and rehabilitation methods. Along with innovative research involving the use of various biologic therapies, novel approaches to diagnostics, and advances in pain recognition and modulation, ESMR clinicians are leading the way to understanding, treating and managing axial skeleton pain and dysfunction. This team is not only researching various approaches for treating injuries but they are also at the forefront of assessing novel methods for monitoring conditioning, training, and injury prevention. Numerous studies are currently underway such as utilization of markerless motion capture in induced lameness models, validation of inertial measurement unit (IMU) and machine learning to gold standard force plate and optical motion capture, and the use of IMU technology to quantify training workload and define the presence of gait asymmetries with performance metrics.

Another recent development has been the creation of the Equine Spine Center (ESC), which is a specialized veterinary collaboration dedicated to the diagnosis, treatment, and rehabilitation of horses with axial skeleton-related conditions. This center will seek to improve the overall well-being and performance of horses via innovative research, diverse educational opportunities, and individualized patient care. By focusing exclusively on equine spinal health, ESC aims to become the global leader in advancing the diagnosis and management of unwanted or dangerous behavior, chronic pain, musculoskeletal impairment, and neurologic deficits in horses.

Equine sports medicine and rehabilitation is an extensive field that requires a very dedicated team of veterinarians, researchers, and barn staff. This annual report highlights some of their important work that is on-going as part of the ORC.



CSU Photography, John Eisele

HIGHLIGHT ARTICLES

From impactful studies performed by the Equine Sports Medicine & Rehabilitation Service

Review of the Mechanism of Action and Use of Bisphosphonates in Horses

A. Yocom, E. Contino, C. Kawcak

Bisphosphonates are a group of drugs that were first developed in the 1960s for the treatment of bone diseases associated with excessive bone resorption. Bisphosphonates reduce bone re-sorption by incorporating into the crystal structure of exposed hydroxyapatite where they are taken up by osteoclasts. They can then decrease osteoclast recruitment, differentiation, and resorptive activity and induce osteoclast apoptosis. There is significant evidence to show that in addition to reducing bone resorption, bisphosphonates also have several other mechanisms of action and can mediate bone pain, alter macrophage function, and reduce inflammation through interactions with immune cells. In humans, bisphosphonates have been used in the treatment of several conditions, including but not limited to Paget disease, myeloma, osteoarthritis, rheumatoid arthritis (RA), bone metastases, osteoporosis in adults, and osteogenesis imperfecta in children.

Horses are predisposed to fatigue-related injuries to their bones and a loss of bone mass or quality secondary to numerous causes including microdamage, trauma, severe lameness, paralysis, age, osteoarthritis, and various genetic abnormalities. Two non-nitrogenous bisphosphonates, clodronate and tiludronate, are FDA approved for the treatment of navicular syndrome in horses. However, these bisphosphonates have also been used off-label in the treatment of other conditions, including silicosis, dorsal spinous process impingement, sesamoiditis, osteoarthritis, and proximal suspensory ligament enthesopathy. In dogs, bisphosphonates have been used in palliative pain management in cases of bone cancer.

Research in several species has shown that in addition to their actions on bone metabolism, bisphosphonates also have pain-relieving, anti-inflammatory, and immune-mediating properties. The positive clinical effects seen from off-label use of bisphosphonates in horses may be due to these properties. However, there remains a gap in our understanding of how bisphosphonates work in horses, especially considering that bisphosphonates are often used in conjunction with other therapies.

Overall, based on this review of the literature, clodronate and tiludronate appear to have significant bone-sparing effects in bones that have been placed into a bone-losing state, whether experimentally induced or naturally occurring. Considering that horses undergo loss of bone as seen experimentally and clinically, it is a sound conclusion that bisphosphonates can have a positive effect in the treatment of those conditions. In addition, compared to the higher potency bisphosphonates, clodronate may show a sparing effect on osteoblastic function and therefore may reduce osteoclastogenesis while sparing bone formation.

The use of bisphosphonates in horses still requires significant research in both juvenile and adult horses. Additionally, research is needed to determine the safety and mechanism of action of bisphosphonates in off-label use instances. In a clinical setting, bisphosphonates are often used in addition to other therapies, so further research will also help to clarify the indications for use of bisphosphonates in horses.

Blind Versus Ultrasound-Guided Low-Volume Perineural Injection of Tibial and Fibular Nerves in Equine Cadaver Limbs

S. Colla, K. Seabaugh, G.M. Zanotto, K. Selberg

Funding: College Research Council, Colorado State University

Techniques for local anesthesia of the tibial and superficial and deep fibular nerves in horses are well established. Ultrasound-guided perineural blocks can identify the nerve location, reduce the anesthetic volume needed and avoid needle misplacement. The aim of this research was to compare the success of blind perineural injection technique to ultrasound-guided technique. Fifteen equine cadaver hindlimbs were divided into two groups. Perineural injection of the tibial and fibular nerves was performed using a mixed solution of radiopaque contrast, saline and food dye. Blind perineural injection (n= 8) used 15 mL for the tibial and 10 mL for each fibular nerve. Ultrasound-guided technique (n= 7) used 3 mL for the tibial and 1.5 mL for each fibular nerve. The limbs were radiographed immediately after injections and sectioned transversally to evaluate the diffusion and presence of the injectate adjacent to the tibial and fibular nerves. The presence of dye immediately adjacent to the nerves was considered a successful perineural injection. No statistically significant difference was observed between groups for success. Distal diffusion of injectate following perineural injection of the tibial nerve was significantly less for the ultrasound-guided technique compared to blind perineural injection. Proximal, distal and medial diffusion of injectate following perineural injection of the fibular nerve was significantly less for ultrasound-guided compared to blind injection technique. Low-volume ultrasound-guided technique results in less diffusion but similar success compared to blind perineural injection, leaving it up to veterinarian preference when selecting a technique.



Figure 1: Radiographs showing the contrast injected in the region of tibial and fibular nerves. Left: Ultrasound-guided perineural injections. Right: Blind perineural injections.

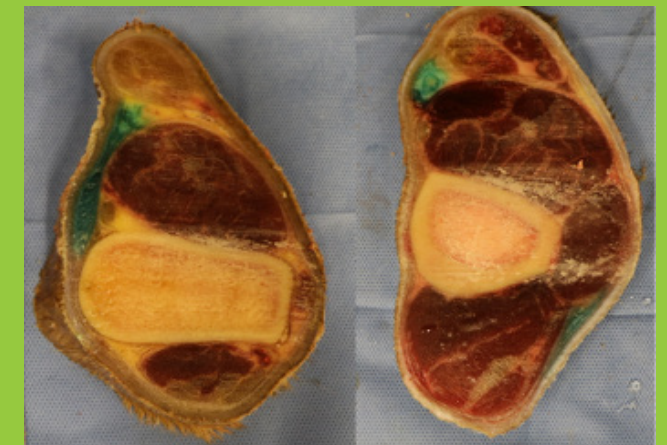


Figure 2: Dye diffusion in anatomical cross-section of tibial nerve region. Left: Blind perineural injection. Right: Ultrasound-guided perineural injection. Note the presence of stain also in the superficial fibular nerve region.

Equine Blood Flow Restriction Training: Safety Validation

S. Johnson, D. Frisbie, G. Griffenhagen, M. King

Funding: Translational Acceleration Program (TAP) of the Translational Medicine Institute

Blood flow restriction (BFR) has become a key rehabilitative tool for human orthopedic conditions. With modernized technology and evolution of clinical application, patient-specific delivery of occlusion percentages is now considered the standard of care in human patients due to improved therapeutic outcomes and minimized safety risks. Safety validation and limb occlusion pressure (LOP) data for horses, however, are lacking. The objectives of this study were (1) to determine if BFR exposure resulted in fore-limb biomechanical gait dysfunction that would manifest as subjective or objective evaluation of lameness for safety validation purposes; (2) to determine inter-horse and inter-limb (left forelimbs compared to right forelimbs) LOP value differences that are currently unknown. Providing this information to clinicians is expected to help guide safe BFR clinical use in the horse.

In this controlled in vivo experiment, daily unilateral forelimb BFR was performed in four horses over 56 days. Clinical examinations and objective gait analyses were performed on Days 0, 28 and 56. Daily LOP values were determined by Doppler evaluation to deliver 80% vascular occlusion at a walk. A linear mixed model evaluated for differences in lameness, kinetic and kinematic gait parameters.

This study resulted in the following findings: there were no significant differences in forelimb lameness (range of Grades 0–2 across all forelimbs), kinematic or kinetic gait parameters over time or between BFR exposed and control (contralateral) limbs ($p > 0.05$). Clinically apparent complications related to BFR such as thrombosis or dermatitis were not appreciated. Significant differences in mean LOP values between various horses ($p < 0.001$) and measured left (204.48 mmHg) and right (173.78 mmHg) forelimbs ($p < 0.001$) were observed. Mean LOP and standard deviation across all readings was 189.1 ± 22.2 mmHg. Because of the small study population, optimal BFR occlusion percentages and protocols with documented clinical efficacy are unknown. Exposure to BFR did not result in forelimb biomechanical dysfunction in four horses. Applied pressures of 75–151 mmHg would likely simulate a range of 50%–80% vascular occlusion in horses, but inherent physiological variation between horses and forelimbs warrants incorporation of individual pressures.



Figure 1: Acquisition of Doppler limb occlusion pressure (LOP) reading in the standing, unsedated horse immediately prior to blood flow restriction walking exercise (A). The blood pressure cuff was inflated using the manual pressure regulator option on the Delfi system, up to the pressure at which the distal pulse was no longer heard. Once the Doppler LOP value was obtained, it was used to back-calculate 80% vascular occlusion pressure that was subsequently applied through the pressurized cuff. Note piezoelectric Doppler probe placement immediately distal to the cuff along the medial aspect of the limb to obtain the pulse of the median artery (B).

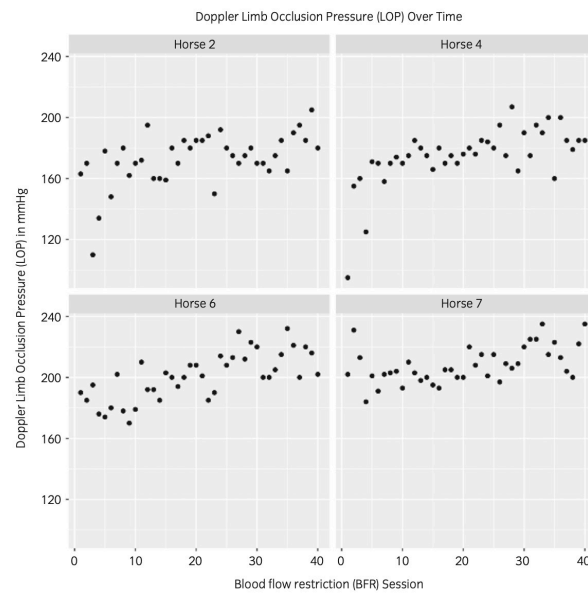


Figure 2 (above): Limb occlusion pressure (LOP) values in mmHg determined via daily Doppler ultrasound evaluation in 4 horses over 40 blood flow restriction (BFR) sessions. Statistically significant differences between horses were noted with variations in daily readings also noted (standard deviation of roughly 22 mmHg across all readings).

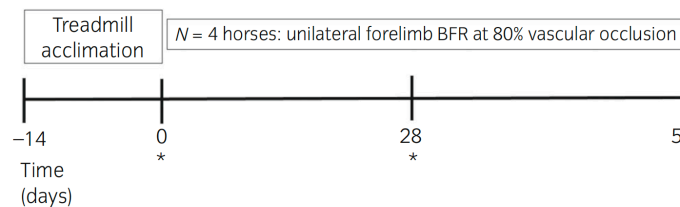


Figure 3 (left): Following 14 days of treadmill acclimation, unilateral forelimb blood flow restriction (BFR) walking exercise at 80% vascular occlusion was performed once/day for 5 days/week for a 56-day study period. On Days 0, 28 and 56, clinical, kinetic and kinematic evaluations were performed (*). Doppler limb occlusion pressure (LOP) readings were obtained daily immediately prior to BFR walking sessions.

BUDGETS

Revenue and Expense

| REVENUE | FY2023 |
|--|--------------------|
| Total Interest | \$764,330 |
| Service Activity Total | \$12,374 |
| Medical Center Clinical Service Total | \$673,209 |
| Research Project Accounts Total | \$4,487,186 |
| Stallion Auction | \$25,823 |
| State Funds Total | \$102,591 |
| Total Donations | \$634,223 |
| TOTAL REVENUE | \$6,699,736 |
| EXPENSE | |
| Total Salaries | \$1,493,846 |
| Faculty Travel | \$13,572 |
| Materials and Supplies | \$365,983 |
| Other Direct | \$592,452 |
| Building | \$3,609 |
| Equipment | \$16,035 |
| Deficit Payments | \$96,002 |
| EXPENSE SUBTOTAL | \$2,581,499 |
| FACILITY AND ADMINISTRATIVE OVERHEAD COSTS | \$298,881 |
| TOTAL EXPENSE AND OVERHEAD | \$2,880,380 |
| ACCOUNT BALANCE | \$3,819,356 |

| REVENUE BREAKDOWN | FY2023 |
|------------------------|------------------|
| INTEREST ON ENDOWMENTS | |
| McIlwraith Scholarship | \$7,825 |
| Cox Anthony Chair | \$168,953 |
| Iron Rose Ranch Chair | \$131,776 |
| Atkinson Chair | \$59,107 |
| Kawanakoa Chair | \$116,839 |
| Malone Chair | \$279,830 |
| TOTAL INTEREST | \$764,330 |

| REVENUE BREAKDOWN | FY2023 |
|--------------------------|------------------|
| STATE FUNDS | |
| Story CRC Grant | \$20,669 |
| Nelson CRC Grant | \$24,995 |
| Pezzanite CRC Grant | \$24,996 |
| Frisbie CRC Grant | \$6,931 |
| Kawcak CRC Grant | \$25,000 |
| STATE FUNDS TOTAL | \$102,591 |

| EXPENSE | FY2023 |
|-----------------------------|--------------------|
| SALARIES | |
| Faculty Salaries | \$546,671 |
| Research Associate Salaries | \$25,480 |
| Administrative Salaries | \$406,736 |
| Residents | \$233,480 |
| Graduate Student Salaries | \$63,534 |
| Hourly Students | \$217,944 |
| TOTAL SALARIES | \$1,493,846 |

FUNDING

Grants

| INVESTIGATORS | SPONSOR | PROJECT TITLE | PERIOD | AMOUNT |
|--|--|--|------------------|-----------|
| Erin Contino, Laurie Goodrich (Co-PIs) | Zoetis | Prospective clinical trial: Evaluation of autologous protein solution (APS) as an anti-inflammatory therapeutic for adult horses with naturally-occurring lameness isolated to the medial femorotibial joint | 1/1/22-12/1/25 | \$315,844 |
| David Frisbie (PI) | College Research Council (CRC) | The effect of blood flow restriction therapy on interleukin-1 receptor antagonist protein and stem cell harvest in horses: a proof of concept study | 7/1/22-6/30/23 | \$6,931 |
| David Frisbie (PI), Myra Barrett, Katie Seabaugh, Brad Nelson (Co-PIs) | The Stone Research Foundation | Stone Foundation paste graft assessment | 6/15/23-6/15/25 | \$395,055 |
| Laurie Goodrich (PI), Brad Nelson, Kirk McKilvrey, Ben Gadomski (Co-PIs) | AlloSource | Comparison of fresh to cryopreserved human osteochondral allografts (COCA): characterization of cellular, biomechanical and structural markers over fresh and extended storage conditions | 8/1/21-12/31/23 | \$151,852 |
| Laurie Goodrich (PI), Parvathy Thampi, Brian Johnstone, Steven Dow, Linda Chow (Co-PIs) | Hong Kong Jockey Club Research Foundation | Immunomodulatory effects of equine chondroprogenitor cells in an animal model of osteoarthritis | 4/1/22-3/30/23 | \$37,935 |
| Laurie Goodrich (PI), David Frisbie, Myra Barrett, Christopher Kawcak, C. Wayne McIlwraith, Constance Chu (Co-PIs) | DOD-US Department of Defense | Development of diagnostic and treatment strategies for post traumatic osteoarthritis (PTOA) | 9/1/18-12/31/23 | \$711,101 |
| Laurie Goodrich (PI) | eQcell | Experimental protocol for co-culture | 7/1/23-6/30/24 | \$108,745 |
| Laurie Goodrich (PI), David Frisbie, Myra Barrett, Christopher Kawcak, C. Wayne McIlwraith (Co-PIs)/Constance Chu (PI) | Stanford University (DOD-US Department of Defense) | Localized gene therapy for prolonged anti-inflammatory treatment to prevent or delay PTOA in an equine model | 1/15/20-1/14/25 | \$952,862 |
| Laurie Goodrich (PI), Kirk McGilvray, Ben Gadomski, Myra Barrett, Katie Seabaugh, Brad Nelson (Co-PIs) | Nanochon | Testing and scale-up of 3D printed cartilage repair device for clinical use | 5/2/22-8/31/24 | \$673,464 |
| Laurie Goodrich (PI), Brad Nelson, Parvathy Thampi (Co-PIs) | Ocean Tunicell | Product development & testing of scaffolds as a repair device for clinical use | 5/15/22-12/31/24 | \$99,952 |
| Laurie Goodrich (PI), Katie Seabaugh, Brad Nelson (Co-PIs) | eQcell, Inc. | eQcell clinical trial- Use of allogeneic umbilical cord blood-derived mesenchymal cells for treatment of synovitis in horses: an efficacy study | 2/1/23-6/1/24 | \$103,005 |
| Laurie Goodrich (PI), Katie Seabaugh (Co-PI) | Mechano Therapeutics | STTR Phase I: Mechanically controlled drug delivery platform for joint environments | 6/15/23-5/31/24 | \$119,924 |
| Laurie Goodrich (PI), Brad Nelson (Co-PI) | Cayman Biomedical | KMNI59 bone stimulation to enhance fracture repair: a pilot study | 9/1/22-8/31/24 | \$113,283 |
| Laurie Goodrich (PI), Brad Nelson, Charlotte Barton (Co-PIs) | American College of Veterinary Surgeons | Tenoscopic-guided resection of the manica flexoria utilizing radiofrequency energy | 12/1/22-11/30/24 | \$12,978 |

| INVESTIGATORS | SPONSOR | PROJECT TITLE | PERIOD | AMOUNT |
|--|---|---|------------------|--------------------|
| Christopher Kawcak (PI), Brad Nelson, Holly Stewart, Kelly Zersen, Kurt Selberg (Co-PIs) | The Foundation for The Horse | Validation of an innovative contrast subtraction technique to detect equine bone marrow lesions using CT | 10/1/20-8/30/24 | \$19,981 |
| Christopher Kawcak (PI), Kurt Selberg, Holly Stewart, Lauren Smanik (Co-PIs) | The Foundation of the Horse | Development of an experimental model of palmar osteochondral disease in the horse: a pilot study | 10/17/22-1/31/24 | \$12,403 |
| Christopher Kawcak (PI), Lauren Smanik, Kurt Selberg, Holly Stewart (Co-PIs) | Grayson-Jockey Club Research Foundation | Development of an experimental model of palmar osteochondral disease in the horse: a pilot study | 4/1/22-3/31/23 | \$15,002 |
| Christopher Kawcak (PI), MC Duff, Xiaochuan Pan, Emil Sidky, Kurt Selberg, Holly Stewart, C. Wayne McIlwraith (Co-PIs) | Grayson-Jockey Club Research Foundation | Development of limited view 3D imaging for the equine distal limb | 4/1/18-3/31/23 | \$198,836 |
| Christopher Kawcak (PI), Steve Simske, Luke Bass, Erin Contino (Co-PIs) | College Research Council (CRC) | Development of a visual AI technique to characterize musculoskeletal pain in horses | 7/1/22-6/30/23 | \$25,000 |
| Christopher Kawcak (PI), Brad Nelson, Lauren Smanik (Co-PIs) | Hong Kong Jockey Club Research Foundation | Development of a CT-based biomarker of the fetlock joint disease | 11/1/23-10/31/26 | \$314,914 |
| Christopher Kawcak (PI), Katie Sikes, Lindsey Burton, Kelly Santangelo, Laurie Goodrich (Co-PIs) | College Research Council (CRC) | Cellular persistence after intra-articular injection using encapsulated pGMB hydrogels | 7/1/23-6/30/24 | \$24,983 |
| Melissa King (PI), Sandro Colla, Katie Seabaugh (Co-PIs) | College Research Council (CRC) | Validation of novel wearable sensor technology | 7/1/23-6/30/24 | \$24,890 |
| Lauren Luedke (PI), Norm Ducharme, Fabrice Rossignol, Ben Gadomski, Jimmy Johnson (Co-PIs) | College Research Council (CRC) | Biomechanical properties of 3 implant techniques for prosthetic laryngoplasty in the arytenoid cartilage of ex vivo equine larynges | 7/1/23-6/30/24 | \$22,387 |
| Brad Nelson (PI), Katie Sikes (Co-PI) | College Research Council (CRC) | Development of an equine chronic tendinopathy model: A more clinically applicable approach for testing emerging therapies | 7/1/22-6/30/23 | \$24,995 |
| Brad Nelson (PI) | Prohibix | Joint safety study of a HYALUTE microparticles: A prolonged action hyaluronic acid | 8/25/23-12/31/24 | \$23,001 |
| Yvette Nout-Lomas (PI), Lisa Bartner, Tawfik Aboellail, Lawrence Whalen (Co-PIs) | College Research Council (CRC) | Electrodiagnostic testing in horses with distal cervical vertebral compressive myelopathy | 7/1/23-6/30/24 | \$24,335 |
| Lynn Pezzanite (PI), Dean Hendrickson, Steve Dow (Co-PIs) | College Research Council (CRC) | Exploring the link between gut dysbiosis and inflammation in progressive osteoarthritis in horses | 10/1/22-9/30/23 | \$24,996 |
| Lynn Pezzanite (PI), Steven Dow, Dean Hendrickson, Laurie Goodrich (Co-PIs) | Grayson-Jockey Club Research Foundation | Transcriptomic response to Osteoarthritis using single cell sequencing approaches | 4/1/23-3/31/25 | \$165,475 |
| Lynn Pezzanite (PI), Lyndah Chow, Steven Dow (Co-PIs) | College Research Council (CRC) | Identifying optimal senolytic drug therapies to treat equine osteoarthritis | 7/1/23-6/30/24 | \$24,920 |
| Lauren Smanik (PI) | Arthrex | CSU ACP Max Bone Study: AIRR-0247 | 11/27/23-5/31/26 | \$40,730 |
| Melinda Story (PI) | College Research Council (CRC) | A cross sectional survey of dorsal root ganglionitis in horses | 7/1/22-6/30/23 | \$20,669 |
| Melinda Story (PI), Kelly Santangelo (Co-PI) | College Research Council (CRC) | Exploring the dorsal root ganglia in a naturally occurring model of osteoarthritis | 7/1/23-6/30/24 | \$25,000 |
| | | | TOTAL | \$4,836,089 |



The Orthopaedic Research Center at Colorado State University is known worldwide for joint problem prevention and healing research in horses, with complementary work in human athletes. We are at the forefront of developing novel therapies, including stem cells that offer exciting treatment options for neuromusculoskeletal disease and injury.

Your gift to the ORC will advance our research program, support innovation in clinical treatments and regenerative therapies, and advance translational research. If you have more questions about giving opportunities at the ORC, please contact Sarah Schmidt, Assistant Vice President of Advancement, at s.schmidt@colostate.edu.

You can also give online at

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