

Zweig

From the Harry M. Zweig
Memorial Fund for Equine
Research at Cornell University
College of Veterinary Medicine



No. 59 June 2015

Pushing Boundaries in Arthritis Prevention



Osteoarthritis is the leading cause of a horse's premature retirement from an athletic career. "Once you start down the pathway of arthritis, there is no good treatment for horses or humans," says Dr. Kyla Ortved, a 2015 Zweig grant recipient. With the help of this funding, Ortved aims to develop a novel treatment using gene therapy that could be used to prevent osteoarthritis in the joints of both horses and humans.

Ortved is Clinical Assistant Professor at Cornell Ruffian Equine Specialists, and has spent much of her research career focusing on gene therapy to improve cartilage repair in the horse. This work translates well to developments in human cartilage repair, as the equine femoral patellar joint is roughly the same thickness as a human's and the weight-bearing properties are quite similar as well. "Horses are a really great preclinical model for this work," says Ortved.

Of course, healing horses is also a major goal of her research, which will comprise using an adeno-associated virus (AAV) vector to insert genes that over-express the anti-inflammatory protein, interleukin-10 (IL-10) into the cells of the joint environment. These cells would adopt this foreign gene into their own coding, and thus begin to produce unusually high amounts of IL-10 themselves. Ortved's hope is that this anti-inflammatory gene vector could be directly injected into the cells of a joint that has had some slight trauma or inflammation, and this boost of IL-10 would act as a



protective and preventative measure against further damage. "The idea is that this could be a method to prevent arthritis from occurring, instead of treating it," says Ortved.

Currently, Ortved is testing her gene-therapy approach on cartilage cells and other joint tissue cells in the lab. "We've already seen that when these cells are treated with IL-10, they are somewhat protected against inflammation," she says. The next step in her research is to look for the same results in explanted cartilage tissue.

The available treatments for osteoarthritis in horses are limited. Anti-inflammatory drugs, such as injected steroids, alleviate pain, but can cause further damage to the joint's cartilage tissue. IRAP therapy (interleukin-receptor antagonist protein) helps block inflammation but has only short-term effects. Ortved's gene therapy approach would avoid the damage of steroids and provide a long-lasting protective effect on the joint.

CORNELL Ruffian Equine Specialists





Harry M. Zweig Memorial Fund For Equine Research 2015 Awards

NEW

\$57,494 to Dr. Johnathan Cheetham for "Regenerative Approach to Recurrent Laryngeal Neuropathy"

\$20,459 to Dr. Lisa Fortier for "Subtle Meniscal Injury as an Initiating Event in the Development of Subchondral Bone Cysts"

\$49,150 to Dr. Robert Gilbert for "Controlled Postponement of Ovulation in Mares"

\$49,933 to Dr. Helene Marquis for "Bacterial pilus as Vaccine Target for Strangles"

\$62,074 to Dr. Alan Nixon for "Enhanced Breakdown Screening in Thoroughbred Racehorses through Multimodal Imaging and Serum Biomarker Combinations"

\$28,814 to Dr. Kyla Ortved for "Harnessing the Immunomodulatory Properties of Interleukin-10 through a Gene Therapy Approach to Prevent Equine Osteoarthritis"

\$50,000 to Dr. Scott Palmer for "Epidemiology Acute Breakdown Study"

\$25,144 to Dr. Rolfe Radcliffe for "En Bloc Removal of Intravascular Thrombi via an Extracorporeal Bypass Circuit in Experimentally Induced Jugular Thrombosis in Horses"

\$80,617 to Dr. Tracy Stokol for "Platelets are a Trojan Horse that Deliver Equine Herpes Virus to Endothelial Cells"

CONTINUED

\$91,920 to Dr. Alan Nixon for "Evaluation of Lubricin as a New Biotherapeutic for Equine Joint Disease"

\$79,841 to Dr. Bettina Wagner for "A Novel Strategy to Boost Antibody of EHV-1 in Neonates"



Zweig Memorial Trot 2015

Vernon Downs, Vernon, N.Y.

Sunday, July 26, 2015

Post Time: 1:15pm

Information: 1-877-888-3766 | www.vernondowns.com/racing

Boosting Knowledge on Nerve Healing

Roaring, or laryngeal paralysis, causes poor athletic performance in horses. Attempts to restore function to the laryngeal muscle have failed due to poor nerve healing. Dr. Joy Tomlinson, a clinical fellow in Dr. John Cheetham's research group, the Preclinical Upper Airway Lab at Cornell University's College of Veterinary Medicine, aims to change that. Through examining the healing effects of specific immune cells on nerve regeneration, Tomlinson hopes to develop novel treatment applications that can be used to help improve the outcomes of nerve graft surgery—an application that could help not only horses, but dogs and humans as well.



Laryngeal paralysis occurs when the nerve that controls the opening and closing of the airway loses function, causing the signature 'roaring' sound when the horse is exercising. Cheetham's team experimented in treating these failed nerves by re-routing and grafting other, healthy nerves onto the muscle that controls the airway. Unfortunately, "nerves aren't very good at healing," says Tomlinson, and getting the re-routed nerve to fuse successfully to the airway muscle can prove difficult.

Thanks to Zweig grant funding, Tomlinson will be investigating the effect of certain immune cells, known as macrophages, on nerve graft healing. Macrophages are white blood cells that can stimulate a range of responses in the body, from inflammation to healing. One class of macrophages, known as M1 macrophages, cause a pro-inflammatory response in the body, while another class, known as M2 macrophages, cause a pro-healing response. Tomlinson's goal is to determine and, if necessary, engineer, the right macrophage response, and then apply the right signals to spark a pro-healing immune response in the nerve graft—thus helping to heal horses with laryngeal paralysis.

During her two-year fellowship, Tomlinson will examine how nerve grafts heal in mouse models that are genetically engineered to produce only either M1 or M2 macrophages. "These experiments may tell us that having a 100% M2 immune response isn't necessarily what you want," says Tomlinson. "Maybe you need some M1 macrophages there to help the process." Tomlinson is also examining the possible mechanisms of communication between these different macrophages and Schwann cells, which are integral to the healing and functionality of the new nerve graft. "Once we have a promising therapeutic in mice, we can translate the research over to dogs and horses and evaluate the responses in those species," says Tomlinson.

This work paves the way for potential therapies in multiple species. "This is a condition that not only affects horses, but also people and dogs," Tomlinson says. "So this work is quite basic, and has the potential for lots of clinical applications."

Zweig : June 2015

The Harry M. Zweig Memorial Fund for Equine Research honors the late Dr. Harry M. Zweig, a distinguished veterinarian, and his numerous contributions to the state's equine industry. In 1979, by amendment to the pari-mutuel revenue laws, the New York State legislature created the fund to promote equine research at the College of Veterinary Medicine, Cornell University. The Harry M. Zweig Committee is established for the purpose of administering the fund and is composed of individuals in specified state agencies and equine industry positions and others who represent equine breeders, owners, trainers, and veterinarians.

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Cornell University & Harry M. Zweig Memorial Fund for Equine Research Celebrates its 35th Anniversary

The Zweig Memorial Fund celebrated its 35th Anniversary at Cornell Ruffian Equine Specialists (CRES) in Elmont, NY, on November 12th and 13th last year. The event included research talks, a facility tour, and a reception followed by the Zweig annual meeting.

Faculty and staff from Cornell University's College of Veterinary Medicine, Ithaca, N.Y., including Drs. Bettina Wagner, Michael Kotlikoff, Austin O. Hooley Dean of Veterinary Medicine, Helene Marquis, Joe Wakshlag, Scott Palmer, Rolfe Radcliffe, and Gillian Perkins, along with Kevin Mahaney and Dave Howe, met their Ruffian colleagues, including Drs. Kyla Ortved, Samuel Hurcombe, Alan Nixon, and other faculty and staff for talks and the reception.

Researchers presented an array of equine-related research projects and lectures, including:

- Dr. Gillian Perkins: "Novel Strategy to Boost Antibody Production against Equine Herpesvirus-1 in Neonatal Foals"
- Dr. Rolfe Radcliffe: "Jugular Thrombosis in Horses: A Novel Treatment Approach"
- Dr. Kyla Ortved: "Gene Therapy to Treat Equine Joint Disease"
- Dr. Helene Marquis: "Investigating the Role of Pili in the Pathogenesis of Streptococcus equi"
- Dr. Scott Palmer: "Putting the Horse First", which discussed breakdowns during racing and possible reasons for fatal breakdowns

In addition, Dr. Samuel Hurcombe gave an overview of the CRES facility, located opposite the backstretch of historic Belmont Park.

The celebration also commemorated the late Dr. Harry Zweig, a distinguished veterinarian whose Memorial Fund for Equine Research promotes equine research at the Cornell University College of Veterinary Medicine.



Anna Zweig Retires from Zweig Committee

Anna Zweig, long-time member and leader of the of the Harry M. Zweig Memorial Fund for Equine Research, announced her retirement from the Zweig Committee at the annual meeting on November 13, 2014. In her farewell speech, she said her late husband, Harry Zweig, would have been very pleased at the success and impact of the Zweig Fund, and thanked past and present committee members for their dedication.

It was time for her to step down, she said, to make way for someone more involved in the daily activities of the Fund, and expressed her pleasure that Dr. Ann Dwyer, DVM, '83, had agreed to serve on the Zweig Committee. Michael I. Kotlikoff, VMD, PhD, Austin O. Hooley Dean of the College of Veterinary Medicine at Cornell University, thanked Zweig for her many years of leadership, noting that the Zweig name would still be represented on the Committee through her son, Brian Zweig, who has been a member since 2007.



Cornell review on newborn foal immunity challenges old assumptions



A newborn foal's immune system functions differently than that of adult horses. This spurred the Grayson-Jockey Club Research Foundation to commission Cornell's Dr. Bettina Wagner, associate professor of Immunology, and Gillian Perkins, senior lecturer of Large Animal Medicine, to write a review of the topic in a recent issue of the *Equine Veterinary Journal*, titled "The development of equine immunity: Current knowledge on immunology in the young horse". It discusses the established fact that neonatal foals are born with an 'immature' immune system, rendering vaccines early in life ineffective. "Conventional vaccines have no effect on antibody production in newborn foals," says Wagner. "We need to know more about the neonatal foal's immune system so that effective neonatal vaccines can be developed."

Wagner and Perkins push the boundary on old assumptions. "This review triggers some of the dogmas that have been around in equine research," says Wagner. "We discuss new immunological explanations for the low responsiveness of neonatal foals to vaccines that was solely blamed on indirect effects of the colostrum for the past fifty years."

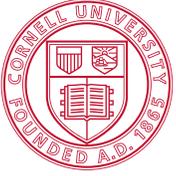
For example, it was believed that the maternal antibodies a foal receives from its mother's first milk prevent neonatal foals from producing their own antibodies. However, the review explains how new research has tracked individual classes of antibodies, proving that some were actually generated before the foal was born. "In addition, several antibody classes are made by the foal in

high amounts, despite maternal antibodies being around. This discovery was a little eye-opening," says Wagner.

Rather than the lack in the ability of making antibodies, Wagner says, it is the lack of T helper-2 cells that causes the foal's incomplete immunity early in life. These helper cells are essential to induce antibodies in response to foreign antigens. Without these cells, the immune response is disabled, making current vaccines non-effective in neonates. Thus, the maternal antibodies are essential for the foal's protection against pathogens and many infectious diseases. "From an immunological perspective, maternal antibodies are an important protective mechanism for foals, but it also makes sense that the foal's immune response is reacting differently from that in adult horses" says Wagner. "Neonates are born from an immunologically protective uterine environment--there are no flies or dirt, no pathogens, and they suddenly enter the outside world with huge amounts of new antigens and immune stimuli. If the newborn immune system were to react as an adult's, it would be a huge reaction--so it's probably healthy for them to learn in little steps."

The review's new perspectives on foal immunity upends conventional assumptions, something Wagner embraces. "We present a different perspective--and it's our hope that this will motivate equine scientists to gain a better understanding on neonatal immunity to develop vaccines that target the immune mechanisms present in neonate foals."

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Please welcome our newest Zweig committee members



Ann Dwyer, DVM, '83

A New York Practitioner, Dr. Ann Dwyer joined the Zweig Committee in 2015. Co-owner of Genesee Valley Equine Clinic in Scottsville, N.Y., Dwyer has practiced at the clinic since graduating from Cornell in 1983. Well known for her expertise in

equine eye diseases, and currently serving as a reviewer for *Equine Veterinary Ophthalmology* and *Equine Veterinary Journal*, she often shares her knowledge and expertise in equine ophthalmology and has published book chapters on the subject. As a past member of Veterinary Management Group 7, she often travels to veterinary schools to share her insights and expertise on accounting, mentorship and veterinary practice management. Dwyer is a member of the American Association of Equine Practitioners (AAEP), the American Veterinary Medical Association, the New York State Veterinary Medical Society, and the International Equine Ophthalmology

Consortium, and she served as President of the AAEP in 2013. Dwyer grew up in Syracuse, N.Y., where she competed in rallies and combined training as a charter member of the Limestone Pony Club. She earned her degree in biology from Mount Holyoke College in 1975. Following college, she worked as a groom and exercise rider at several Florida and East Coast racetracks heightening her interest in veterinary medicine and inspiring her to earn her DVM from Cornell University College of Veterinary Medicine in 1983. Dwyer has been a steady source of service and leadership since joining the AAEP in 1984, and has long been a supporter for the health and welfare of the horse.

Mr. Ronald Ochrym: Acting Director,
Division of Horseracing & Pari-Mutuel Wagering
New York State Gaming Commission

Have you visited our Web site lately?

www.vet.cornell.edu/zweig

This site provides information on the projects and publications resulting from the Zweig Memorial Fund, and demonstrates the objectives of the Fund in promoting equine health in the racing industry.

The Zweig News Capsule is published twice a year, and can be downloaded in PDF format at <http://bit.ly/ZweigNews>
Please encourage other equine enthusiasts to visit this site.