

# Zweig

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



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## Zweig Researcher Spotlight: Dr. Julia Felipe



Dr. Julia Felipe

Dr. Julia Felipe, associate professor of large animal medicine, was the first Harry M. Zweig Assistant Professor in Equine Health. Her research program, which has been funded by Zweig, an NIH Director's New Innovator Award, USDA NIFA, and Morris Animal Foundation, studies equine immunology. Specifically, her work covers equine fetal and neonatal immune development; neonatal response to vaccines; immunodeficiencies in young and adult horses; hematopoietic regenerative medicine, and immunity to infectious diseases (specifically, *Rhodococcus equi* and equine herpesvirus). She also runs the only lab studying common variable immunodeficiency in horses. Her scientific, educational, and clinical work have significantly impacted veterinary and equine medicine. "There is so much to unveil with the immune system of the horse," says Felipe. "That means plenty of opportunities for investigation and discovery."

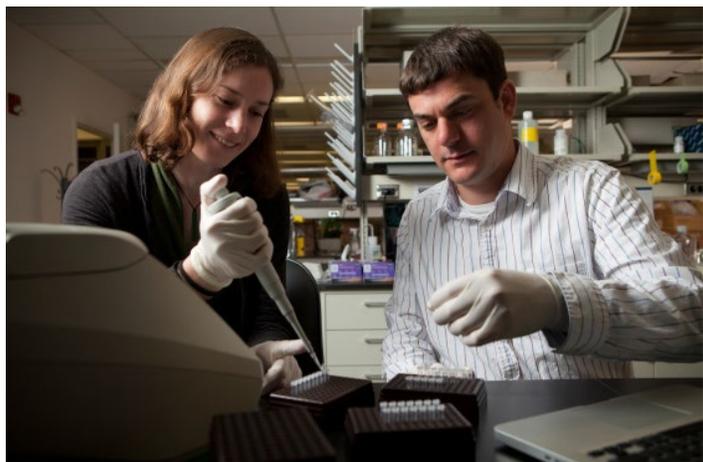
Felipe studied veterinary medicine at Universidade Estadual Paulista in Botucatu, Brazil. After a few years practicing in horse breeding farms and evaluating (and riding) endurance horses, she traveled to Kansas State University College of Veterinary Medicine, where she completed an internship in equine surgery and medicine,

a Master's degree in veterinary science, and a residency in equine internal medicine. Later she would come to the Cornell University College of Veterinary Medicine to study as an immunology graduate student under Dr. Doug Antczak, the Dorothy Havemeyer McConville Professor of Equine Medicine at the Baker Institute of Animal Health. "During my residency, I looked for the best training I could get in equine immunology, and I was fortunate to be able to join Dr. Antczak's research program," says Felipe.

Felipe is now head of the Equine Immunology Laboratory at the College, which has undertaken many innovative research investigations and accomplished several scientific 'firsts': Felipe's group is (to their knowledge) the first to study epigenetic mechanisms of disease in the horse and to promote differentiation of equine hematopoietic stem cells into B cells *in vitro*. They are also the only laboratory to perform bone marrow transplantation in a horse with common variable immunodeficiency, and measure the diversity of the equine antibody response to vaccines. Recently, with Research Associate Dr. Rebecca Tallmadge, the group has tested an epigenetic modifier to control equine herpesvirus infection *in vitro*. "Innovation is always part of breakthrough research," says Felipe, "but having a team that complements knowledge, experience and enthusiasm is key, and Dr. Tallmadge has brought this strength to our program for many years."

Felipe has also contributed significantly to teaching and clinical service; she's written and published the first Equine Clinical Immunology book, and runs an immunologic testing service for horses through her lab. "While on clinics in our College teaching hospital, learning with students and residents, or discussing cases with veterinarians, I feel that the loop is complete," Felipe says. "Clinical cases feed our curiosity and research program, our discoveries help clinical cases, and we share this knowledge to move the field forward."

# Roaring in horses may be tied to height



Dr. Adam Boyko (right)

Researchers have identified a genetic factor associated with recurrent laryngeal neuropathy (RLN), or “roaring” in horses. The Zweig-funded research comes with both good and bad tidings. The good news? Scientists can now predict which horses are more susceptible to the disease by looking at their genes. The bad news is that the genetic factor associated with RLN is closely tied to a favorable gene that increases height at the withers.

This finding may explain why RLN is particularly prevalent in tall horse breeds: the disease can affect up to 46% of draft horse breeds and 2-11% of Thoroughbreds. The condition paralyzes the left side of the larynx, which obstructs air flow and dramatically reduces athletic performance. Surgical interventions or retirement are currently the only options for diagnosed horses.

Scientists have long suspected that RLN had a genetic component, however, the exact genes responsible for the disease were unknown. This was until Dr. Adam Boyko, professor of Biomedical Sciences at the College of Veterinary Medicine,

well-known for his work on dog genetics, identified a genetic variant that increases the probability of developing RNL. “(Professor of Large Animal Medicine) Dorothy Ainsworth approached me, and it was a great research question— I was excited to help out,” says Boyko. “The genomic techniques we use in my lab on dogs are the same techniques that were used for this project.”

According to Boyko, one of the most surprising and unexpected results of this study was that the genetic signal associated with RLN seemed to coincide with a gene known to increase height. This means that breeding to reduce RLN prevalence may lead to shorter adult size in horses.

But Boyko is not discouraged and he does not plan to stop there. The researcher explains that the overlapping signal for horse height and RNL does not mean that both genes are one and the same. There is a possibility that both genetic factors are located very close to each other in the genome, but still distinct. “I’ve got no plans to shift my lab away from dogs, but I do think using multiple domesticated species, dogs, horses, cats, etc., enables some really interesting comparative analyses,” Boyko says. “Working with Tracy Stokol and Dorothy Ainsworth, I’m hoping that Cornell continues to be on the cutting edge of equine genetic mapping.”

Even if RNL and height have a common genetic component, further studies may also reveal other genetic factors that act as “modifiers,” attenuating RLN risk without reducing size or performance. “I’m very appreciative of the Zweig foundation’s support of my research, and the foresight to support genetic work that will ultimately help to reduce the prevalence of heritable diseases in horses,” says Boyko. — *By Elodie Gazave*

## Zweig Trot: July 24, 2016

Bar Hopping and Flowers N Songs (pictured right) proved victorious in their respective main events of the Dr. Harry M. Zweig Memorial for harness racing 3-year-old trotters on July 24 evening at Vernon Downs. Flowers N Songs is pictured with retired Zweig committee member Mrs Anna Zweig, current committee member Dr. Scott Palmer, and Cornell faculty and staff.



# Cloning hepatitis virus in horse may save human lives



Maxx, the horse that was instrumental to Cornell's NPHV clone research

Scientists have produced an infectious copy, or clone, of a horse virus called Nonprimate hepacivirus (NPHV). The NPHV clone, developed in collaboration with Cornell researchers, could provide crucial insights into human hepatitis C, a disease that chronically affects 2% of the world population and for which there is currently no vaccine.

“NPHV infection causes mild or no clinical symptoms in horses,” says Dr. Thomas Divers, Steffen Professor of Veterinary Medicine at Cornell University, and one of the Cornell scientists who oversaw the experiment. On the contrary, hepatitis C is a devastating disease that can develop into cirrhosis and liver cancer.

HCV exclusively reproduces in human and chimpanzee cells, making it hard to study in animal models. To make matters worse, there are almost no related viruses that naturally infect domestic animals. It was only in 2012 that a US-UK team including Professor of Virology Edward Dubovi at Cornell University discovered the NPHV in horses. Because NPHV and HCV are so similar, the discovery of NPHV was a promising step to understand the human disease. However, to study NPHV in controlled conditions and perform experimental infections, researchers needed to establish hepacivirus cultures, and growing equine liver cells in conditions that allow the NPHV virus to replicate has so far proved unsuccessful.

Using the genetic sequence of NPHV as a template, an international team, composed of researchers from Denmark, the Rockefeller University, the Research Institute at Nationwide Children's Hospital, along with Zweig-funded researchers at Cornell University, created an artificial copy, or clone of the virus that would not need to be grown in cells.

To demonstrate that the clone was infectious and similar to the natural NPHV, the team injected the clone into the liver of a horse called Maxx. After two weeks, Maxx became positive for NPHV antibodies and although asymptomatic had mildly elevated liver enzymes associated with the infection. After 19 weeks, no sign of the infection was detectable in Maxx's body. “Maxx tolerated well the procedure. He never missed a meal, he did not show any discomfort,” says Dr. Bud Tennant, Emeritus James Law Professor of Comparative Medicine, who participated in the study.

The success of NPHV cloning has opened new research horizons for the study of hepacivirus in horses, and may be a useful model for human hepatitis C vaccine development. – *By Elodie Gazave*

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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