

Zweig

NEWS CAPSULE

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

Advancing vaccines

This year another outbreak of equine herpesvirus type-1 (EHV-1) swept through the United States in May, affecting 90 reported horses and killing 13. Cases of herpesvirus Myeloencephalopathy (EHM), a neurological disease caused by EHV-1, have increased so sharply in number and mortality over the last five years that the USDA recently classified EHM as an emerging infectious disease.

The virus can spread through air, nursing, and contact with infected animals, equipment, or hands. It remains in hosts for life, flaring up during times of stress or weak immunity to cause respiratory disease, abortion, and in the case of EHM, brain disease, paralysis, or death. Treatment, quarantines, lost training and competition time, and deaths pose enormous costs to equine industries worldwide.

“Vaccines induce strong antibody responses but only offer partial protection,” said Dr. Bettina Wagner, immunologist at the Animal Health Diagnostic Center at the College of Veterinary Medicine, where she leads the first team to study horses’ innate immune responses to EHV-1. “We need to understand how the virus interacts with the immune system in order to develop vaccines that effectively bolster horses’ abilities to build immunity.”

Wagner’s Zweig-funded research recently produced two papers published in the journal *Veterinary Immunology and Immunopathology*. They describe how EHV-1 keeps innate immune cells from producing crucial chemokines and cytokines, proteins that trigger and modulate the adaptive immune system to create specially-tailored T-cells designed to combat the virus and prevent severe clinical disease.



“Currently we are working to show that EHV-1’s ability to subdue innate immune responses prevents the host from developing enough adaptive T-cells to combat the virus,” said Wagner. “We are also exploring the factors that increase an infected horse’s susceptibility to neurological disease. We think that reduction of the body’s T-cell population plays a major role in causing EHM.”

Older horses seem to be more frequently affected with neurological signs and fatal outcome of disease than foals, and part of Wagner’s study explores how and why susceptibility to EHM increases with age. “If we can find out what immunological factors help protect younger horses from neurologic disease we can use this knowledge to develop vaccines to boost similar responses and offer increased protection,” said Wagner.

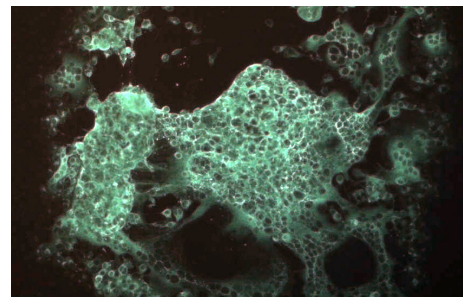
To fully understand how EHV-1 decreases protective immunity, Wagner also investigates which viral genes enable EHV-1 to manipulate immune systems. “We need to know how the virus interacts with the immune system and what genes drive those interactions,” said Wagner. “This will help us adapt new vaccines that can more effectively combat EHV-1.”

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Herpesviruses affect nearly all vertebrate species, including all major livestock and companion animals. Human medicine has struggled to develop vaccines against the eight known herpesviruses that can infect people. Understanding how the horse immune system interacts with equine herpesvirus could help inform parallel herpesvirus research and vaccine development to protect people and other animals from these increasingly common infectious diseases.

(Right: cells infected with EHV-1)



Behind the scenes with Scott Baxendell

Rolling farmland spread across the 165-acre Equine Research Park at Cornell hosts between 75 and 100 horses. Farm Manager Scott Baxendell oversees the park's two locations and many facilities, including a broodmare barn, stallion barn, breeding shed and lab, quarantine barn, several paddocks, pastures, and run-in sheds where horses live.

Along with several temporary employees and three full-time staff, Baxendell runs the Park's quarantine and breeding services and manages horses for research and teaching.

"I've been involved at the Park since it first began," said Baxendell. "I started as an Animal Sciences student in '81. After graduation in '83 I worked in my family's landscaping business until the College's Dean, Dr. Franklin Loew, called and asked me to apply for a position opening at the Park."

Baxendell started as an Animal Technician in '86 and spent more than 20 years managing the Annex side of the Park and

its USDA-approved quarantine facility where imported horses are tested for contagious equine metritis (CEM).

"Any horse from Europe or other CEM-affected countries needs to be quarantined for 20 days and tested for CEM," said Baxendell. "The College's Department of Clinical Sciences and the Animal Health Diagnostic Center help operate this service. We have one of the few facilities equipped to handle CEM cases, and though all our tested horses have come out clear, we have had two stallions sent here specifically for treatment."

When the Park's former Director of Equine Services Carol Collyer retired last year, Dr. Lorin Warnick asked Baxendell to step up and assume her position as Farm Manager, now with a year under his belt.

"Our mission is to give students more hands-on experience with horses," said Baxendell. "Horses at the park support the teaching and research missions at the veterinary college and in Cornell's Animal Sciences department, where students benefit tremendously from interactions with animals."

Often students will take the initiative to set up appointments and come out to learn more. Baxendell and his staff help set up practice physical exams, and professors sometimes come out to demonstrate proper clinical techniques.

"Exposure to normal horses gives students a sense of what is abnormal," said Baxendell. "That can be critical when it's time to diagnose. Students value these opportunities. My favorite part of the job is working with the horses and with the people who come here to work and learn with them."



To rebuild degrading joints

Many equine athletes develop traumatic joint problems, which often limit potential and shorten a career. Joint injuries and subsequent osteoarthritis cost the equine industry as much as \$100 million annually.



Dr. Alan Nixon, professor of orthopaedic surgery and director of Cornell's Comparative Orthopaedics Laboratory, has been charting the mechanism of arthritis development to identify targets for early treatment of cartilage and joint disease. Degrading cartilage stimulates the body to produce inflammatory proteins that accelerate the destruction. With support from the Zweig Fund, Nixon's research group has developed a line of stem cells designed to silence these inflammatory proteins and stimulate cartilage regrowth.

"Last year we found we could effectively silence erosive proteins in arthritis using a process called RNA interference. Loading stem cells with these gene-based silencing systems provides an anti-inflammatory progenitor cell that can be injected into the joint to seed the lining and provide long-term internal control of the arthritic cascade. This could potentially rebuild tissue to restore function in affected joints."

Previous studies funded through Zweig in 2009 documented the pro-inflammatory proteins involved in knee arthritis following chip fracture and other trauma. The group currently studies how stem cells primed with genes that silence these proteins can reduce lameness and joint swelling after knee chip-fracture in racehorses.

"We are designing stem cells that bolster cartilage regrowth in the hostile environment of a damaged joint," said Nixon. "It is not enough to just inject stem cells into the joint and hope for the best; we now know this provides few if any of the building blocks required for robust cartilage repair. We expect stem cells can be more effective when they bolster the local cartilage cell progenitor pool and concurrently quell inflammation."

Nixon's group explores both sides of the delicate balance in joint surface maintenance and repair and will evaluate long-term improvement in previously arthritic joints treated with this new therapy. "We plan to explore additional targets for gene silencing and combine several major developmental genes to drive cartilage cell formation in these 'armored' stem cells," said Nixon. "We are nearing application in clinical patients with joint trauma and early arthritis, which will be a milestone in treatment for one of the more serious set-backs to our equine athlete."

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 Harry M. Zweig Memorial 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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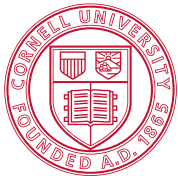
Middlebrook Farm

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Zweig Memorial Trot
PANTHOLOPS

August 29, 2011
One Mile Trot

Owner: Menhammar Stuteir
Trainer: Jonas Czernyson
Driver: Andy Miller

Race: 5
Time: 1:56:4



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