

Zweig

Memorial Fund News Capsule

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



Courtesy of the United States Trotting Association

For a quarter century, the Zweig Fund has made possible research to improve the health, welfare, and performance of racehorses.

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- ▶ Julia Flaminio Seeks Ways to Stimulate Foal's Immune System

Zweig Fund Celebrates Its Twenty-Fifth Year

Dr. Harry M. Zweig was a veterinarian in Nassau County whose untiring efforts played a vital role in the passing of the 1965 Laverne Law. This legislation provided the groundwork for the New York Sires Stakes program. Thanks to Zweig, harness racing in New York flourished. Under his guidance in the mid-1960s, a two-afternoon non-pari-mutuel meet was expanded into a weeklong pari-mutuel event held at the New York State Fairgrounds in Syracuse. Later the \$150,000 Empire Open Trot was added.

When Zweig died unexpectedly in 1977, the New York State Legislature paid tribute to his efforts by establishing the Harry M. Zweig Memorial Fund for Equine Research as a source of financial support for basic and practical equine



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research to be conducted at Cornell University's College of Veterinary Medicine.

On this 25th anniversary of the fund's establishment, the Zweig Committee that administers the fund takes pride in its research accomplishments.

Here are some of the highlights.

One of the first equine performance testing clinics in North America was established thanks to Zweig funds.

Cardiopulmonary Research

Thanks to Zweig funding, researchers at Cornell have made great strides in better understanding roaring, exercise intolerance, bleeding, chronic obstructive pulmonary disease (COPD), exercise-induced hypoxia, lung infections, and edema in exercising horses.

In 1987, Richard Hackett, DVM, MS, Dipl ACVS, and Norm Ducharme, DMV, MSc, Dipl ACVS, established one of the first equine performance testing clinics in North America. Projects undertaken in the clinic have improved the diagnostic accuracy of poor performance using minimally invasive techniques; established the Cornell laryngeal grading system (now used worldwide); and developed a now widely accepted technology to measure tracheal airway pressure.

In 2003, many years of research culminated in the development of the laryngeal tie-forward, a surgical method to treat horses with dorsal displacement of the soft palate. In collaboration with Brett Woodie, DVM, MS, Dipl ACVS, Hackett and Ducharme also developed an equine throat support—an external device that prevents palate displacement during exercise. It is now being marketed.

In the early 1990s, pulmonologist Dorothy Ainsworth, DVM, MS, PhD, Dipl ACVIM, began to examine the vital role that the diaphragm plays in exercising horses. As exercise intensifies, she's found that electrical activity increases, which helps generate more pressure to bring air into the lungs. Her work has shown that neither the "visceral piston" (the liver and abdominal contents) nor the concussive forces of foot plant contribute significantly to airflow during exercise.

In 2003, with Judy Appleton, PhD, and Doug Antczak, VMD, PhD, Ainsworth studied the effects of high-intensity exercise on pulmonary immune responses in young horses and the immunological basis of heaves.

Between 1992 and 1995, Alan Dobson, PhD, and Robin Gleed, BVSc, MRCVS, DVA, Dipl ACVA, adapted a technique from human medicine to measure how lung water accumulates during exercise, contributes to hypoxemia, and compromises performance. They showed that exercise substantially increases the pressure in the capillaries of the lung but does

not significantly increase water in the lung. As a consequence, it does not contribute to the hypoxia that compromises performance. Along with Hackett, Dobson and Gleed also developed techniques to measure bronchial artery blood flow in exercising horses in order to better understand the causes of bleeding (exercise-induced pulmonary hemorrhage).

Reproduction

Studies initiated in 1990 through 1992 allowed Joanne Fortune, MS, PhD, and her team to describe patterns and regulation of follicular development during the equine estrous cycle and have developed a protocol to reliably trigger double ovulations three times more often than normal. This advance makes embryo transfer more practical.

Barry Ball, DVM, PhD, learned how sperm survive and how the embryo triggers signals to the mare to recognize and support the pregnancy. To reduce the rate of late pregnancy loss, Peter Daels, DVM, PhD, learned



that nonsteroidal anti-inflammatory drugs (NSAIDs) are not effective in preventing premature contractions, but that doubling the recommended dose of a synthetic progesterone does prevent them. Working with Patrick Concannon, MS, PhD, Daels also found that by giving horses sulpiride and keeping them indoors under artificial photoperiods for 12 to 22 days, breeders can better time their horses' ovulation.

The work of Dietrich Volkmann, BVSc, MMed Vet, Dipl ACT, in 2002, focused on hormonal patterns and the role of endometrial cups in mares affected by Mare Reproductive Loss Syndrome. His findings will help researchers better understand the mechanisms that cause the devastating pregnancy losses associated with this syndrome. Such knowledge could lead to safe and effective interventions to help mares reconceive more quickly after pregnancy loss.

In 1992, Katherine Houpt, VMD, PhD, Dipl ACVB, found that the attachment of a mare to her foal declines with time, whereas the foal is more attached to its dam in the third week of life than at an earlier age. Thereafter the foal's attachment to the mare also declines.

Orthopedics

Zweig funding has long supported projects to reduce bone and joint problems: among these are studying muscle morphology and gait analysis, developing tests for diagnosing osteoarthritis, perfecting surgery to repair bowed tendons, and creating implants to repair cartilage defects and prevent arthritis.

To help repair and minimize—or even reverse—arthritic changes in damaged joints, Alan Nixon, BVSc, MS, Dipl ACVS, developed implants that promote cartilage growth. These now are commonly used to treat cartilage disease in horses and are being tested for use in humans. Most recently, Nixon has been applying gene therapy to repair cartilage damage. Nixon uses modified viruses to carry useful genes such as growth factors. These implants enhance cartilage production and joint-lining function and stimulate the formation of new cartilage over time. Thus, the implants treat

not only generalized joint disease but also specific cartilage injuries. Current work combines the types of genes that stimulate new cartilage growth with those that quell the arthritic reaction that drives joint disease through its most painful stages.

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Drs. Susan Fubini, DVM, Dipl ACVS, Hollis Erb, DVM, PhD, and Rory Todhunter, BVSc, PhD, Dipl ACVS, worked together to examine what risk factors, for all horses presented to the Cornell University Hospital for Animals (over a seven year period) with joint disease, contributed to soundness and short- and long-term survival. This information helps owners and trainers make more informed decisions when faced with a horse with joint disease.

In 2000 and 2001, Kevin Haussler, DVM, DC, PhD, designed a new instrument that allows scientists, for the first time, to measure the motion between two individual vertebrae in the live horse. Zweig funding provided the opportunity to better understand the effects of muscle and joint injuries on the equine back. The work not only helps researchers better understand the causes of equine back problems and their effects on locomotion and performance, but also allows them to develop ways to objectively evaluate the effects of chiropractic treatment on back pain and stiffness.

Infectious and Genetic Diseases

Zweig grants have helped scientists better understand the causes and/or treatments for equine protozoal myeloencephalitis, equine degenerative myeloencephalitis, equine arteritis virus, Potomac Horse Fever, Equine Motor Neuron Disease, and Equine Rhabdomyolysis (commonly known as "tying up" or "Monday Morning Disease").

Much progress has been made in developing or improving vaccines for equine influenza, strangles, Lyme disease, and leptospirosis. Between 1979 and 1988, Dorothy Holmes, DVM, PhD, successfully developed two long-lasting nasal-spray equine influenza vaccines.

Between 1997 and 1998, Yung-Fu Chang, DVM, PhD, and Thomas Divers, DVM, Dipl ACVIM, Dipl ACVECC, experimentally produced Lyme disease in horses. They improved the diagnosis and treatment of Lyme disease by determining which antibiotics are most effective. In a vaccine trial in ponies, they found that an OspA recombinant vaccine could induce protection against Lyme infection and disease.

In 2001, Chang made a breakthrough toward the development of a vaccine for leptospirosis by pinpointing and isolating certain surface proteins from a virulent strain of the bacteria that are critical for infection and immunity but do not cross-react with the eye.

Since his appointment in 2002, Klaus Osterrieder, DVM, Habilitation (a degree equivalent to a PhD), has focused on developing an effective vaccine for equine herpes virus type 1 (EHV-1). He successfully identified a gene that expresses a protein that makes one strain of the virus virulent but is absent from strains that do not cause a disease state. He believes that this mutant strain will prove useful for a vaccine.

Amy Glaser, DVM, PhD, is working on developing a new lab test to diagnose the devastating West Nile Virus. Dwight Bowman, MS, PhD, has been studying equine protozoal myeloencephalitis (EPM) since it was identified in 1991. (EPM is responsible for more than 35 percent of all equine spinal cord disease in the United States.) Bowman's work with Divers has helped disprove a theory about the causes of the disease in horses.

Nutrition and the Gastrointestinal System

Another of Houpt's Zweig studies in 2002 found that cribbing (the behavior in which a horse grasps a horizontal



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surface with its teeth and swallows air) can be reduced by feeding the horse hay only, or hay and oats, rather than mixed grain and molasses. Since 2000, Robert Gilmour, PhD, has studied the mechanisms by which cisapride and domperidone improve intestinal motility to treat post-operative ileus. He is testing the hypothesis that blocking ERG channels (the ion channels that allow potassium to exit cardiac muscle and GI smooth muscle cells) may be an important mechanism for enhancing gut motility.

Zweig funding has supported the development of a linkage map for the horse, which pinpoints particular regions on a chromosome that carry genes for specific traits—such as running speed or disease susceptibility.

Basic Research

One of the greatest recent achievements, between 1996 and 2003, has been the rapid progress made on the horse genome. Cornell's contribution is under the guidance of Doug Antczak, VMD, PhD. Zweig funding has supported the development of a linkage map for the horse, which pinpoints particular regions on a chromosome that carry genes for specific traits—such as running speed or disease susceptibility.

So far, more than 500 markers have been mapped. These markers indicate the order and placement of genes on chromosomes; they provide insights into which traits are inherited together. About 500 more are currently being characterized. In addition, more than 300 genes have

been mapped on the physical map and more than 3,000 genes have been sequenced.

Practical applications have only just begun to emerge. Researchers have already developed genetic tests to identify severe combined immunodeficiency disease (SCID), hyperkalemic periodic paralysis (HYPP), and lethal white disease so that breeders can prevent potentially troublesome stallion-mare pairings. Much more promises to follow—even for complex conditions that may be nonhereditary but involve gene expression, such as understanding the causes of and improving treatments for conditions including laminitis, developmental bone diseases, and colic.

“The Zweig fund has been very important in kick-starting the careers of many young faculty members who have gone on to be very successful,” notes Antczak. “Overall, the Zweig fund has really put Cornell on the map as a destination for students, post-docs, and faculty who wish to conduct research on important problems of the horse.” ■



Alaxis Werski-Roberts, The Image Lab

Profile: Dr. Julia Flaminio

Before Julia Flaminio, DVM, PhD, Dipl ACVIM, was an equine immunologist, an assistant professor of large animal internal medicine, and a veterinary judge for national and worldwide competitions in trail and endurance riding, she worked on breeding farms in her home country of Brazil. As a resident veterinarian, Flaminio used artificial insemination and embryo transfer techniques and treated neonates in distress. She became increasingly interested in the health problems of the young foal.

"In the initial phase of life, the foal is very vulnerable to infections," Flaminio explains. "The horse placenta does not allow transfer of antibodies during gestation, so the foal is born essentially devoid of antibodies. The immune system of the very young horse can respond to organism insult, but it needs time to develop and become fully competent."

Certain problems kept raising questions in Flaminio's mind until she became too curious to stay in private practice.

She acquired additional training, first at the University of Pennsylvania School of Veterinary Medicine, then at the College of Veterinary Medicine at Kansas State University.

"During my residency, I was motivated by even more questions, especially about how the immune system elaborates a response and how we can modulate that response," says Flaminio.

She was awarded a PhD in 2002 in immunology from the College of Veterinary Medicine under the mentorship of Doug Antczak, VMD, PhD. She then joined the faculty in the College of Veterinary Medicine as an assistant professor with expertise in equine immunology.

Her research focuses on the development of the equine immune system in the fetus and in the young foal. With a new Zweig grant, Flaminio is seeking to lay the foundation for developing ways to stimulate the immune system of very young horses.

"We're trying to identify areas of the foal's immune system that are well developed so we can target them to facilitate the immune response and make it more protective," she explains.



Nicola Kountoupes/University Photography

Julia Flaminio's interest in the health problems of young foals began when she was a practicing veterinarian in her native Brazil.

She is currently looking at adjuvants, the parts of vaccines that aren't derived from pathogens but that promote the attraction and activation of immune cells to recognize and process foreign particles.

"We're trying to identify areas of the foal's immune system that are well developed so we can target them to facilitate the immune response and make it more protective."

—Julia Flaminio

"We want to determine if the same adjuvant that's been effective in inducing an immune response against viral and bacterial organisms in neonates and adults in other species will prove helpful in assisting foals prepare their immune system during the first few weeks of life, when they most need it," Flaminio explains.

In another area of research, Flaminio is trying to identify the causes of an acquired immunodeficiency in adult horses that she has recently identified and is currently characterizing. In addition, she has been collaborating with Klaus Osterrieder, DVM, Habilitation, and Amy Glaser, DVM, PhD, in the development of vaccine strategies for Equine Herpes Virus-1 and West Nile Virus.

Flaminio is already co-author of more than 20 peer-reviewed articles, 19 scientific abstracts, and seven book chapters—mostly on immunomodulation and immunology of the horse. She also writes for the lay reader. Almost a dozen of her articles on care of horses, riding tips, and other aspects of endurance riding have been published in horse journals and magazines. In addition, Flaminio serves as a worldwide veterinarian judge for championship endurance competitions.

"I am absolutely delighted that Dr. Flaminio has chosen to join the Department of Clinical Sciences," says department chair Richard Hackett, DVM, MS, Dipl ACVS. "She is a superbly trained clinician and scientist with a passion to improve equine medicine. Her enthusiasm for her research, her teaching, and her clinical work is fantastic." ■

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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