

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

Bloodstream battles

When bacteria bloom in the blood the ensuing battle can wreak havoc on the body. Endotoxemia, bacterial blood poisoning, ignites a rising tide of immune cells and blood platelets that help fight infection but can also cause tissue damage. In horses, endotoxemia and subsequent inflammation can cause severe complications following abdominal surgeries, in common equine disorders including colic and retained placenta, and in weak foals that fail to nurse properly.

Dr. Thomas Divers is leading a team of Cornell veterinarians investigating a new approach to treating the effects of endotoxemia by quelling the rampaging immune response. Collaborators Drs. Marjory Brooks, Susan Fubini, Ashlee Watts, Tracy Stokol, and Sally Ness aid in the investigation.

"Veterinary clinicians currently use a 'best guess' approach to managing horses with endotoxemia," said Divers. "They typically administer a broad spectrum of treatments to clear bacteria and support cell repair, but specific attempts to block the inflammatory response have mostly failed. We have developed a new strategy for treating endotoxin that targets blood platelets as a key control point."

If successful, this novel approach will change the bestguess strategy into an evidence-based solution to suffering by using the anti-platelet drug clopidogrel (Plavix®), one of the most commonly used drugs in human medicine. The project will provide insights into the pathophysiology of endotoxemia and the ability of Plavix® to down-regulate platelet reactivity in endotoxic horses.



"Plavix® is a highly effective oral anti-platelet agent, and holds promise for helping treat inflamed horses," said Divers. "We have optimized techniques to evaluate equine platelet reactivity, forming a testing panel broadly applicable for investigating thrombosis in horses, particularly in studying laminitis. We are now performing anti-platelet drug treatment trials for horses with endotoxemia. The trials are going well, and we are looking forward to publishing by the end of the year. When the patent on Plavix® expires in 2012, generic versions of the drug will become available, and we will be poised to start using anti-platelet drugs to affordably and effectively treat blood poisoning and inflammation in horses."

2011 Research Awards

New

\$82,250 to Dr. Dorothy Ainsworth for "The Genetic Basis for Recurrent Laryngeal Neuropathy (RLN) in Thoroughbreds"

\$43,914 to Dr. Jonathan Cheetham for "Diagnosis of Poor Performance in Racehorses"

\$30,000 to Dr. Thomas Divers for "Targeting Platelets as a New Treatment Strategy for Endotoxemia"

\$44,646 to Dr. Lisa Fortier for "Determining Anti-Nociceptive and Matrix Restorative Mechanisms of Platelet Rich Plasma in Osteoarthritis" \$63,271 to Dr. Bettina Wagner for "Innate Immune Mechanisms and T-Cell Responses to Equine Herpesvirus Type 1 in Latently Infected and Naïve Horses"

Continuation

\$57,213 to Dr. Lisa Fortier for "Optimization of Platelet Rich Plasma Components for the Treatment of Tendonitis"

\$101,065 to Dr. Alan Nixon for "Targeted Delivery of Stem Cells for Pro-Inflammatory Cytokine Suppression in Arthritic Joints"

Executive Director Gordon joins Zweig Committee

The Trustees of the Agriculture and New York State Horse Breeding Development Fund unanimously selected former N.Y.S. Assemblyman Tim Gordon of Bethlehem, N.Y., as the Fund's newest Executive Director. As directed by N.Y.S. law, the executive director also serves as a standing committee member for the Harry M. Zweig Memorial Fund for Equine Research.

"I'm delighted to answer the call to serve on the Zweig committee," said Gordon. "As New York's largest industry, agriculture is central to our state's economic development. The Agriculture and New York State Horse Breeding Development Fund keeps and creates jobs here in New York and continues to be effective because the Fund rewards success.

"In addition to advancing the Zweig Committee's mission, it is my hope to elevate awareness and appreciation here and beyond the continent that horses bred in New York are superb, so that when you ask someone to name three great horse breeding states, New York is included in the answer."

Each of the Trustees thanked Mr. Gordon's predecessor, Peter Goold, for his service to the Fund over the past eight years.



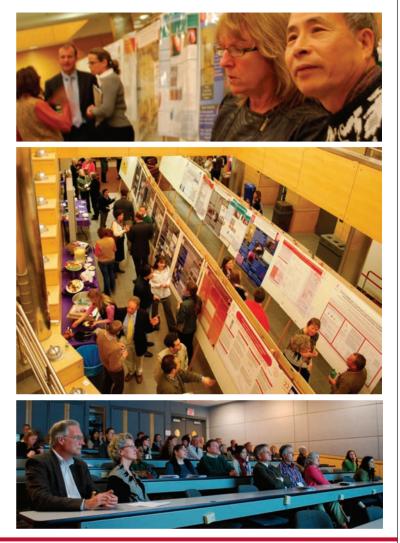
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Poster session highlights research

Faculty, post-docs, and graduate student researchers presented on the College's equine-related research projects in a series of posters and lectures on November 18, 2010, at the Veterinary Education Center. The College-wide event was attended by members of the committee administering the Harry M. Zweig Memorial Fund for Equine Research, who came to see and learn about progress and discoveries in equine research conducted at the College of Veterinary Medicine and to find possible candidates for future support.

Speakers included associate professors Dr. Lisa Ann Fortier and Dr. Maria Julia Felippe from the Department of Clinical Sciences, with their respective lectures on "Platelet Rich Plasma Treatment of Sports Medicine Injuries" and "Epigenetics: A Novel Approach in Primary Immunodeficiencies."

Research scientist Dr. Jonathan Cheetham of the Equine Testing Clinic followed with his talk, "Early Diagnosis and Treatment of Upper Airway Disease in Horses." Margaret Brosnahan, DVM, Ph.D candidate, ended with her lecture, "A New Road to Discovery: Equine Research in the Post-Genome Era."



Zweig archived

Need to check a back issue (or a current issue) of the Zweig Memorial Fund *News Capsule*? Flower-Sprecher Veterinary Library and the College Research Office recently worked together to upload all 50 Zweig *News Capsules* into eCommons, the Cornell University Library digital repository.

Issues from no. 1, 1988 through no. 50, November 2010, are now permanently preserved and accessible electronically at any time directly at the library's eCommons site or via Cornell's Library Catalog. Recent issues will still be available on the Zweig website.

Issues on eCommons are full-text searchable, arranged by date, and are tagged with selected descriptors that include research award listings by year. For instance, if you want

to find incidences of "Saratoga" or "treadmill" in the text of any of the issues, simply entering the desired words in the search box will quickly narrows results.

In 1993, efforts to present Zweig research were captured through a video presentation highlighting research studies conducted at the College. It can be found in the subject list under its title, "Champion Results," or under "video."

It is possible to set up RSS (Really Simple Syndication) feeds from the collection via any RSS newsreader, such as Google Reader, and receive alerts when new issues are posted in eCommons. The collection may be found at http://ecommons.library.cornell.edu/handle/1813/22528

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Pregnancy paper picked by biology elite

A paper on pregnancy immunology from the lab of Dr. Doug Antczak has been selected by the Faculty of 1000, placing his work in a library of the top two percent of published articles in biology and medicine.

According to its website, the Faculty of 1000 (F1000) identifies and evaluates the most important articles in biology and medical research publications. Articles are selected by a peer-nominated global faculty composed of the world's leading scientists and clinicians who rate chosen articles and explain their importance.

Antczak's paper, "Functions of ectopically transplanted invasive horse trophoblast," (*Reproduction* 2011 Mar. 9), was selected and evaluated by F1000 member Anthony Michael Carter.

"This paper advances understanding of how invasive trophoblast cells are able to establish endometrial cups in the mare," wrote Carter in an evaluation describing Antczak's discovery. Trophoblast cells, which form around embryos, can migrate to the uterus. In pregnant mares, these invading cells form ulcer-like structures in the uterus that produce equine gonadotropin. This hormone serves several functions in pregnancy including protecting the embryo from the mother's immune system. "Our work may have practical application in equine practice, for example in the development of new methods to prevent unwanted estrus in competition mares," said Antczak. "It also has implications for biomedical use in the future, as a way to provide sustained delivery of biologically active molecules or drugs."

The project's lead scientist, Dr. Amanda de Mestre, was formerly a post-doctoral fellow in the Antczak lab, and is now a faculty member at the Royal Veterinary College in London. De Mestre's training included two distinct experiences at Cornell. While still a veterinary student in her native Australia, she spent a summer conducting research in the Antczak lab as a participant in Cornell's Leadership Program.

F1000's database provides both a repository for peer-rated high-impact biology articles and a social media forum for serious science. Its community features enable discussions to be built around the selected publications. Additional faculty members may evaluate and rate the article, and subscribers can post comments. Antczak will be able to join the conversation, providing follow-up notes concerning his article and responding to ideas put forth by commenters and evaluators.



"As a post-publication peer review service, we embrace the idea that the impact of your article can deepen and spread in unforeseen ways with community interaction," wrote Sarah Greene, Editor in Chief of the F1000, in a letter to Antczak announcing his inclusion. "Even your own reckoning of the article may advance toward further conclusions and result in new strategies and collaborations."

This research is part of a continuing program in equine pregnancy immunology at the Baker Institute for Animal Health that has been supported for many years by the Zweig Memorial Fund, the Dorothy Russell Havemeyer Foundation, and the National Institutes of Health.

Website updated with fresh look

The Zweig website at www.vet.cornell.edu/public/research/zweig/index.htm has taken on a new look. The site provides information on the projects and publications that have resulted from funding by the Zweig Memorial Fund and demonstrates the objectives of the Zweig Memorial Fund in promoting equine health with regard to the racing industry. Please encourage equine enthusiasts to visit the site.

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Grayson Storm Cat Award

Catherine Hackett, DVM, Ph.D., has been selected as the winner of the 2010 Storm Cat Career Development Award. The \$15,000 award is presented to an earlystage scientist with an interest in a career in equine research.

Selected from numerous competitors, Hackett's research will focus on equine stem cells in a project entitled "Temporal Analysis of Mesechymal Progenator Cells." The research will be overseen by Dr. Lisa Fortier, a distinguished researcher, recipient of multiple Grayson-Jockey Club



Research Foundation grants, and frequent recipient of Zweig funding.

"My project investigates characteristic cell surface traits of cell populations in bone marrow, particularly the cells that can form tissues such as cartilage, bone, and muscle," said Hackett. "I look at the surface of different cell types to determine what type of mature cells they will become, such as blood or bone cells. I also study how these surface properties change over time in culture as the cells grow and respond to culture conditions."

For patients waiting for stem cell therapy, it can take time (e.g. four to eight weeks) for cultured stem cells to divide enough times to reach clinically useful numbers. Hackett hopes to find ways to both decrease the time needed in culture before cells are ready to be implanted and to improve the ability of cells to form the correct tissue

"Stem cells from bone marrow have been used in horses to help heal injuries to tendons, cartilage, and joints, improving repair and changing the patient's immune response to transplantation of cells or tissues from a different donor," said Hackett. "The same applications are being investigated in humans to treat similar types of injuries as those seen in the horse. The properties of mesenchymal stem cells are still poorly understood, and we hope our research into their characteristics and behavior can help find ways to improve their clinical utility and function."

The award is named for the Thoroughbred stallion Storm Cat, which stood at Overbrook Farm in Kentucky. Overbrook is owned by the family of Lucy Young Hamilton, a Foundation board of directors member who personally underwrites the Career Development Award. 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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