



2016 Harry M. Zweig Memorial Fund for Equine Research Summary Report for the Web

The 2016 Annual Report covering the period of January 1, 2016 through December 31, 2016 is provided herein.

For this reporting period, The Harry M. Zweig Memorial Fund for Equine Research Committee granted approval for 6 of 11 submitted projects. Six were new studies, plus three continuations awards were also approved. The total amount allocated for 2016 awards was \$429,242. Reports are provided herein. *Lay summaries are provided for the public website in a separate document.*

Additionally, the Veterinary College hosted its 8th annual poster session celebrating the collaboration between the Harry M. Zweig Memorial Fund for Equine Research and Cornell University College of Veterinary Medicine. Participants included Cornell faculty, students, and scientific staff showcasing their research to the community and the Zweig Committee, including talks and a poster session on Wednesday, November 16, 2016, followed by a meet and greet reception.

2016 Harry M. Zweig Memorial Fund for Equine Research Awards

<u>CONTINUATION</u>		<u>ANNUAL AWARD</u>
Dr. Gilbert	Controlled Postponement of Ovulation in Mares (Year 2)	\$50,250
Dr. Nixon	Enhanced Breakdown Screening in Thoroughbred racehorses through Multimodal Imaging and Serum biomarker Combinations (Year 2)	\$62,715
Dr. Stokol	Platelets are a Trojan Horse that Deliver Equine Herpes Virus to Endothelial Cells (Year 2)	\$82,514

<u>NEW/Renewal</u>		<u>ANNUAL AWARD</u>
Dr. Felipe	Reducing Equine Herpes Virus viral Load and Recurrence through Epigenetic Control (1 year award)	\$58,702
Dr. Fortier	Macrophage Regulation of Mesenchymal Stem Cell Function (1 Year award)	\$63,887
Dr. Mohammed	Factors Predisposed to Musculoskeletal Injuries and Catastrophic Events in Racing Horses (2 year award)	\$72,661
Dr. Nixon	Arthritis Control through Dual Axis Lubricin Over-Expression and Catabolic Cytokine (1 year award)	\$100,000
Dr. Wagner	Effects of Equine Herpesvirus (EVA) Vaccination Frequency on Host Immunity to EHV-1 (2 year award)	\$84,750
Dr. Van de Walle	Defining the Relationship between Equine Herpesvirus and Development of the Equine Gastric Ulcer Syndrome (EGUS) (1 year award)	\$49,242

FURTHER SECURED FUNDING FROM ZWEIG AWARDS IN 2016

The Incentive Program enables the Fund to leverage its investment in Zweig-sponsored research by encouraging Veterinary College faculty to seek either additional or supplementary monies from external sponsors that base their award decisions on a process that involves informed scientific review. The external grant must be closely related to a Zweig project. Eligible sponsors include, but are not limited to, the Grayson Foundation, the NIH, the NSF, and the USDA's National Research Initiative. Recipients provide an annual report on the use of these funds.

The following external grant awards resulted from Zweig funding:

Principal Investigator	External Award	Sponsor	Project Period	Awarded Amount	Incentive Award
Dr. Norm Ducharme	Thyro-Hyoid Muscle Training to Treat DDSP	Grayson-Jockey Club	2/1/15-1/31/18	\$197,973	\$5,000
Dr. Lisa Fortier J. Cassano	Macrophage Regulation of Mesenchymal Stem Cell Functioning Tissue Regeneration	Morris Animal Foundation	3/1/16-7/1/16	\$81,334	\$5,000

PUBLICATIONS

Lubricin/proteoglycan 4 increases in both experimental and naturally occurring equine osteoarthritis

Reesink HL, Watts AE, Mohammed HO, Jay GD, Nixon, AJ

<http://www.sciencedirect.com/science/article/pii/S106345841630214X> (2017)

Bone marrow concentrate and platelet-rich plasma differ in cell distribution and interleukin 1 receptor antagonist protein concentration

Cassano J, Kennedy J, Ross K, Fraser E, Goodale M, Fortier, L.

<https://www.ncbi.nlm.nih.gov/pubmed/26831858> (2016)

Antibody and cellular immune responses of naïve mares to repeated vaccination with an inactivated equine herpesvirus vaccine

Wagner B, Goodman L, Babasyan S, Freer H, Torsteinsdottir S, Svansson V, Bjornsdottir S, Perkins G.

<http://www.sciencedirect.com/science/article/pii/S0264410X15012530> ((2016)

Equine herpesvirus type 1 (EHV1) induces alterations in the immunophenotypic profile of equine monocyte-derived dendritic cells

Claessen C, De Lange V, Huang T, Ma G, Osterrieder N, Favoreel H, Van de Walle G.

<http://www.sciencedirect.com/science/article/pii/S1090023315005237> (2016)

The development of equine immunity: Current knowledge on immunology in the young horse **Perkins G, Wagner B.**

<http://onlinelibrary.wiley.com/doi/10.1111/evj.12387/full> (2016)

Reduction of thoroughbred racing fatalities at New York racing association racetracks using a multi-disciplinary mortality review process

Palmer S, McDonough S, Mohammed H.

<https://www.ncbi.nlm.nih.gov/pubmed/28613116> (2017)

Lubricin/proteoglycan 4 increases in both experimental and naturally occurring equine osteoarthritis

Reesink H, Watts A, Mohammed H, Jay G, Nixon A

<http://www.sciencedirect.com/science/article/pii/S106345841630214X> (2016)

Transesophageal ultrasound and computer tomographic assessment of the equine cricoarytenoid dorsalis muscle: Relationship between muscle geometry and exercising laryngeal function

Kenny M, Cercone M, Rawlinson J, Ducharme N, Bookbinder L, Thompson M, Cheetham J.

<http://onlinelibrary.wiley.com/doi/10.1111/evj.12561/pdf> (2015)

Equine Mesenchymal Stromal Cells from Different Sources Efficiently Differentiate into Hepatocyte-Like Cells

Pennington Matthew R., Curtis Theresa M., Divers Thomas J., Wagner Bettina, Ness SallyAnne L., Tennant Bud C., and Van de Walle Gerlinde R.

<http://online.liebertpub.com/doi/10.1089/ten.tec.2015.0403> (2016)

Neonatal Immunization with a Single IL-4/Antigen Dose Induces Increased Antibody Responses after Challenge Infection with Equine Herpesvirus Type 1 (EHV-1) at Weanling Age.

Wagner B, Perkins G, Babasyan S, Freer H, Keggan A, Goodman LB, Glaser A, Torsteinsdóttir S, Svansson V, Björnsdóttir S.

<https://www.ncbi.nlm.nih.gov/pubmed/28045974>

Guarino C, Asbie S, Rohde J, Glaser A, Wagner B.

Vaccination of horses with Lyme vaccines for dogs induces short-lating antibody responses

<https://www.ncbi.nlm.nih.gov/pubmed/28668566> (2017)

Galectin-3 Binds to Lubricin and Reinforces the Lubricating Boundary Layer of Articular Cartilage

Reesink HL, Bonnevie E, Liu S, Shurer C, Hollander M, Bonassar L, Nixon A.

<http://www.nature.com/articles/srep25463> (2016)

Neonatal Immunization with a Single IL-4/Antigen Dose Induces Increased Antibody Responses after Challenge Infection with Equine Herpesvirus Type 1 (EHV-1) at Weanling Age **Claessen C, Favoreel H, Guanggang M. Osterrieder N, De Schauwer C, Piepers S, Van de Walle R**

<http://www.sciencedirect.com/science/article/pii/S0378113514005860>

Gerlinde Van de Walle, DVM, Ph.D.
Harry M. Zweig Assistant Professor in Equine Health 2017-2019



Gerlinde Van de Walle and Farrah at the Baker Institute's McConville Barn.

At the November 17, 2016 Harry M. Zweig Memorial Fund for Equine Research annual meeting, in recognition of her success in research related to the health of horses, Dr. Gerlinde Van de Walle was named the third Harry M. Zweig Assistant Professor in Equine Health at the College of Veterinary Medicine, Cornell University. The three-year assistant professorship is effective January 1, 2017 through December 31, 2019.

The intent of the Harry M. Zweig Assistant Professorship in Equine Health is to support a junior faculty member showing promise and productivity in promoting equine health. The honor would be granted for a period of up to three years.

[Dr. Van de Walle's equine research program](#) focuses on infectious diseases and wound healing, work that has been funded by the [Zweig Memorial Fund](#), [Boehringer Ingelheim](#), the [National Institutes of Health](#), the [United States Department of Agriculture](#), the [Cornell Stem Cell Program](#), and the [American Quarter Horse Foundation](#). The results promise to not only help improve the health and wellbeing of horses, but of humans and other animal species as well.

In her infectious disease work, Dr. Van de Walle examines the possible roles of viruses in two common conditions in horses: ulcers and hepatitis. Gastric ulcers are particularly widespread among racing horses, and it has long been suspected this is due to the stressful experiences of training, travel, and the track. Dr. Van de Walle's work has uncovered evidence that an infectious cause may be to blame for at least some of these cases, a possibility that offers new treatment options or even a cure, says Dr. Van de Walle. "If we can link ulcers to an infectious cause we can treat these affected horses and heal them," she says.

In the case of hepatitis, Dr. Van de Walle investigates the ways in which nonprimate hepacivirus (NPHV) causes liver inflammation. Given the close relationship between NPHV and hepatitis C virus, which causes disease in humans, these studies could lead to benefits for both species.

When it comes to wounds, horses often heal quite slowly, particularly on their lower legs. Dr. Van de Walle has been testing stem cells to determine whether they could aid the wound healing process in tissue samples in the lab. Their results show that the substances secreted by stem cells can prevent thick, lumpy scarring (called proud flesh) from forming and also reduce the severity of existing scars. Dr. Van de Walle plans to carry the work forward to testing in horses, and to examine how those treatments may be used in wound management for other animal species, including humans.

The Zweig Assistant Professorship presents her and her research team of graduate students and postdoctoral associates with the opportunity to have a greater impact on the health of these animals, which have always had a unique and powerful relationship with humans. *"The support from the Zweig Memorial Fund is a great foundation; it puts us in a strong position to launch our research into the broader scientific community," says Dr. Van de Walle.*

Jonathan Cheetham, VetMB, PhD, DipACVS
2013-2016 Harry M. Zweig Memorial Fund for Equine Research
Principal Research Scientist Award

At the November 15, 2012 Annual meeting, Dr. Jonathan Cheetham was appointed as the first *Zweig Research Scientist 2012-2013 (reappointed through June 30, 2016)*.

The Zweig Principal Research Scientist is an exceptional recognition and honor for an early career investigator. It was recognized beyond Cornell and many collaborators and scientists asked Dr. Cheetham about it. This gave him the opportunity to talk about the tremendous impact that the Zweig Memorial support has on equine research at the College of Veterinary Medicine at Cornell University. This award has allowed him to start to pursue a line of investigation and development that will lead to regenerative therapies for equine laryngeal disease.

The ongoing, long-term project will produce a fundamental shift in the way in which horses are treated for Recurrent Laryngeal Neuropathy (RLN), or “Roaring”. This is a significant performance limiting problem in both racehorses and sports horses. In recent years and with support from the Zweig Fund, leveraged into support from the Grayson Jockey Club, Dr. Cheetham’s laboratory has made considerable progress towards understanding the etiology of RLN and making an early diagnosis before terminal fibrotic changes occur. This work is currently under review for publication.

The latest techniques and approaches were presented in abstract form at the Neuroscience meeting in November 2013. Dr. Cheetham’s laboratory’s first papers on each of the approaches have been accepted for publication. This work would not have been possible without support from the Harry M Zweig Memorial Fund. In summary, with support from the Zweig foundation he has identified macrophages migrating to the site of nerve graft as a key target to improve outcomes after nerve graft. His group has characterized gene expression changes in these macrophages produced by deletion of genes that control the type of macrophages at the injury site. He has specifically targeted genes that are relevant to nerve repair.

To assess the functional consequences of these changes he has developed two novel approaches that allow quantification of outcomes following a change in macrophage phenotype and has used these methods to assess the downstream remodeling effects of changing the type of macrophages at the injury site. In this process he has identified a target for immunomodulation which when altered promotes recovery in both mice and rats. His group is currently investigating the mechanism of this effect. Working with a team of engineering students he has begun to develop an immunomodulatory nerve wrap that will promote nerve repair. Over the next two years his team hope to test the efficacy of this nerve wrap to promote recovery after nerve graft to the recurrent laryngeal nerve in horses with induced recurrent laryngeal neuropathy. This approach would eliminate the need for tie back which although moderately successful can be associated with dysphagia and coughing. This work is also applicable to human peripheral nerve injury which affects 350,000 Americans a year and to Geriatric Onset Laryngeal Paralysis in dogs.

Thanks to the Zweig Committee.

Jonathan Cheetham VetMB PhD DipACVS
Associate Professor
Department of Clinical Sciences
College of Veterinary Medicine

CORNELL CLINICAL FELLOW IN EQUINE HEALTH

At the 2007 Annual meeting, the Harry M. Zweig Committee approved the allocation of funds to help support a Cornell Clinical Fellow in Equine Health. Dr. Sophy Jesty was selected as Cornell's first Clinical Fellow, followed by Dr. Sarah Pownder, and more recently another individual has been identified as a Clinical Fellow, Dr. Joy Tomlinson and supported in part by Zweig funds, and all have been highly successful. Cornell's College of Veterinary Medicine's two-year Clinical Fellows Program is the first in the country to address a growing shortage of academic veterinarians who conduct research on animal diseases and basic biology.

The program is designed to help students meet the financial and time demands of qualifying for a position in veterinary academic medicine, which has traditionally required students to complete an M.S. or Ph.D. after they finish their doctorate in veterinary medicine (DVM). The two-year program, available to veterinarians who have completed a three-year residency, offers an annual salary of \$65,000 plus benefits and an additional \$15,000 per year to fund a research project.

Zweig Researcher Spotlight: Dr. Joy Tomlinson

Dr. Joy Tomlinson research associate in the lab of Dr. Gerlinde Van de Walle, the 2017 Harry M. Zweig Assistant Professor in Equine Health, is working with colleagues on research that may lead to better treatment and screening for Theiler's disease in horses, and a system for developing a hepatitis C vaccine for humans. <https://ecommons.cornell.edu/handle/1813/51542>

OUTREACH 2016

Patent updates (on-going)

During 2016 patent 9,366,671 "Novel Immunogenic Proteins of Leptospira" patent was issued to Dr. Y-F Chang on 6/14/16 (US). Including; UK (EP244728); Germany (60347502.7); Europe (2447278), Canada (2820949), Germany (60347502.7), France (EP2447278); US (93,366,671) Canada (9,176,133) 11/3/15, and United Kingdom (EP2447278 on 4/8/15. Applicant: College of Veterinary Medicine, Cornell University, Ithaca, NY (2016)

Converted patent application No. 62/216,010 (US); submitted 9/9/2015; "Multiplexing and Enhancing Serological Assays via Cytokine Fusion Proteins." Inventor: B. Wagner; Applicant: College of Veterinary Medicine, Cornell University, Ithaca, NY (2015)

Provisional patent application No. 61/903,619 (US); submitted 11/13/2013; "Stimulation of Neonatal Immunity". Inventors: B. Wagner, G. Perkins; Applicant: College of Veterinary Medicine, Cornell University, Ithaca, NY (2013).

Patent application No. 6465-02PC (submitted 9/6/13) -- "A Method to Induce Protection and Immune Alertness in Neonates". Inventors: B. Wagner, G. Perkins, College of Veterinary Medicine, Cornell University, Ithaca, NY (2014) Patent PCT/US14/651 was issued to Dr. Wagner on November 12, 2014.

Zweig News Capsules

There were two issues of the Zweig News Capsule published in 2016 (61 & 62). Copies of these issues can be found in Appendix (E).

All Zweig News Capsules can be found at the Zweig Website at:
<http://www.vet.cornell.edu/zweig/>

SUMMARY OF EXPENDITURES

The 2016 Summary of Allocations was presented and approved at the Zweig Committee Annual Meeting in November 2016 (Appendix B).

2017 ZWEIG PROGRAM

Eight (8) projects were approved for funding, from a roster of eleven (11) applications, at the Harry M. Zweig Memorial Fund annual November 2016 meeting. The list of projects funded for 2017 are shown in (Appendix D).

APPENDIX A

Summaries 2016 Funding



Dr. Felipe	Reducing Equine Herpes Virus Viral Load and Recurrence through Epigenetic Control
Dr. Fortier	Macrophage Regulation of Mesenchymal Stem Cell Functioning Tissue Regeneration
Dr. Mohammed	Factors Predisposed to Musculoskeletal Injuries and Catastrophic Events in Racing Horses
Dr. Nixon	Arthritis Control through Dual Axis Lubricin Over-Expression & Catabolic Cytokine Antagonism
Dr. Wagner	Effects of Equine Herpesvirus (EVA) Vaccination Frequency on Host Immunity to EHV-1
Dr. Van de Walle	Defining the Relationship between Equine Herpesvirus & Development of Equine Gastric Ulcer Syndrome (EGUS)

**Harry M. Zweig Memorial Fund
for Equine Research - 2016**

P.I.:	Dr. Julia Felipe
Title:	Reducing Equine Herpes Virus Viral Load and Recurrence through Epigenetic Control
Project Period:	1/1/16-12/31/16
Reporting Period	1/1/16-12/31/16

TITLE: Reducing Equine Herpes Virus Viral Load and Recurrence through Epigenetic Control

PRINCIPAL INVESTIGATOR(S): *Julia Felipe*

Equine herpesvirus 1 (EHV1) is a ubiquitous and highly contagious pathogen that causes a range of disease severity from mild rhinopneumonitis to abortion, neurologic disease, and death. Notable outbreaks in recent years have emphasized the potential virulence of EHV1, the limitations of current vaccines, and ensuing economic impacts. The **broad objective** of this research is to identify treatments that will 1) significantly decrease EHV1 viral load, and consequent pathology and shedding during lytic infection; 2) complement antiviral drug efficacy during EHV1 infection; and 3) inhibit EHV1 reactivation from latency. The **immediate objective** of this project is to evaluate the potential of epigenetic drugs to modulate EHV1 infection because EHV1 gene expression is regulated by epigenetic mechanisms, primarily through histone modifications. Sustaining a repressive epigenetic state through inhibition of histone demethylation has been shown to effectively limit human α -herpesviruses *in vitro* and *in vivo*¹⁻³. This outcome was observed both during lytic infection and reactivation from latency. Our **hypothesis** is that maintaining a repressive epigenetic state on the EHV1 genome will decrease viral load during lytic infection, and prevent reactivation from latency. Thus, we propose the following specific aims using *in vitro* systems:

Aim 1) to determine how histone demethylase inhibition decreases EHV1 viral load and gene expression during lytic infection;

Aim 2) to determine how histone demethylase inhibition decreases EHV1 reactivation from latently infected cells;

Aim 3) to determine the epigenetic state of the EHV1 genome in the presence or absence of histone demethylase inhibition

We intend to prepare a manuscript describing these results. We submitted a competitive renewal application for the Harry M. Zweig Memorial Fund for Equine Research to extend these initial findings

These results were presented in a abstract poster format by the Veterinary Investigator Program (VIP) student Emilija Zygelyte at the 2016 Merit-NIH National Veterinary Scholars Symposium, Ohio State University, Columbus, OH.

Abstract: Emilija Zygelyte, Tallmadge RL, **Felippe MJB**. Demethylase inhibitor reduces equine herpesvirus-1 expression *in vitro*.

**Harry M. Zweig Memorial Fund
for Equine Research - 2016**

P.I.:	Dr. Lisa Fortier
Title:	Macrophage Regulation of Mesenchymal Stem Cell Function
Project Period:	1/1/16-12/31/16
Reporting Period	1/1/16-12/31/16

TITLE: Macrophage Regulation of Mesenchymal Stem Cell Function
PRINCIPAL INVESTIGATOR(S): *Lisa Fortier*

Mesenchymal stem cells (MSCs) have the therapeutic potential to treat a wide variety of inflammatory and degenerative disease processes; however, little is known about how the recipient environment, the injured tissue into which the stem cells are delivered, affects the identity and function of the transplanted MSCs.

Although MSCs can turn into many cell types of many tissues including joint, muscle, and nerve, contemporary evidence suggests that the regenerative effects of MSCs are through their ability to effectively improve the local environment rather than to serve as a cell source for new tissue. MSCs secrete numerous factors thought to produce the therapeutic effect through modulation of the injury reparative process and decreasing the immune reaction at the level of the local environment. Several studies have investigated how transplanted MSCs affect the injured recipient environment, but a large knowledge gap remains concerning the recipient environment effects on MSC function. In this proposal, we will determine how the environment regulates MSC identity, and the functional ability of MSCs to decrease the detrimental effects of inflammatory cells present in the damaged tissue targeted for therapeutic MSCs transplantation.

This proposal has direct clinical implications because depending on the environment where they are residing, or into which they are implanted, MSCs can increase or decrease inflammation. In the body, signals from the damaged tissue environment regulate the response of macrophages, which are white blood cells naturally found in injured tissue sites that can facilitate tissue repair or inflammation. MSCs can elicit changes in macrophage function in damaged tissue, but it is not understood how macrophages impact the function of MSCs. In disease states where inflammatory macrophages predominate, such as in an osteoarthritic joint or inflamed tissue such as a tendon, ligament, or muscle, signals secreted from those macrophages have the potential to change the function transplanted MSC from regenerative to pro-inflammatory. If pro-inflammatory macrophages alter transplanted MSC function, a further inflammatory reaction could be elicited rather than the intended regenerative effect. To harness the full capacity of MSCs for regenerative medicine approaches, an understanding of how the transplantation/recipient environment affects MSC function is critical.

***Harry M. Zweig Memorial Fund
for Equine Research - 2016***

P.I.:	Dr. Hussni Mohammed
Title:	Factors Predisposed to Musculoskeletal Injuries and Catastrophic Events in Racing Horses
Project Period:	1/1/16-12/6/30/17
Reporting Period	1/1/16-12/31/16

TITLE: Factors Predisposed to Musculoskeletal Injuries and Catastrophic Events in Racing Horses

PRINCIPAL INVESTIGATOR(S): *Hussni Mohammed*

The broad objective of our proposed study is to identify factors that predispose horses to the risk of musculoskeletal injuries (MIs) and catastrophic events (CEs) during racing at the New York State Thoroughbred Racing Tracks (NYSTR) with the aim of recommending cost-effective strategies to mitigate the associated losses. This objective will be addressed through the following systematic and complementary specific aims: 1) determine the incidence and nature of MIs and CEs among horses racing at the NYSTR as well as the associated factors; 2) identify modifying factors that predispose horses to this risk of MIs and CEs; and 3) examine the concentrations of hyper-phosphorylated neurofilaments (pNF-H) as biological marker for neuronal injuries and a predictor of predisposing factor to racetrack injuries while accounting for the role of oxidative stress.

**Harry M. Zweig Memorial Fund
for Equine Research - 2016**

P.I.:	Dr. Alan Nixon
Title:	Arthritis Control through Dual Axis Lubricin Over-Expression and Catabolic Cytokine
Project Period:	1/1/16-12/6/30/16

TITLE: Arthritis Control through Dual Axis Lubricin Over-Expression and Catabolic Cytokine

PRINCIPAL INVESTIGATOR(S): Alan Nixon

Joint trauma and subsequent osteoarthritis (OA) remain significant injuries in racehorses and the aging human population. Arthritis is second only to tendon and ligament injury as the leading cause of racehorse retirement. Moreover, there are no treatments that markedly alter the progression of OA, and most therapies have focused on symptom-modifying treatments, including analgesics and physical therapy, with end-stage disease typically resulting in arthrodesis or joint replacement, and often concurrent retirement from an athletic career. Lubricin has been investigated as a potential new biotherapeutic that may replace hyaluronic acid (HA) as an injectable for equine joint disease. The aims of the proposed research are to propagate and clone equine lubricin, test its expression in articular cells, combine it with a previously developed attenuated adenovirus expressing interleukin-1 receptor antagonist, and test the combined construct for dual expression and impact in a carpal chip osteoarthritis model. The long-term goal is to prevent the progression of osteoarthritis (OA) through gene-mediated lubricin supplementation combined with suppression of the degradatory and inflammatory master controller, interleukin-1. The broad objectives of this proposal are to develop a dual effector approach to resolution of joint disease in equine athletes. Our previous Zweig grant determined the biophysical organization of lubricin on articular cartilage, the partnering role of the galectins, and the levels and location of lubricin in joint trauma and osteoarthritis. These studies suggest that lubricin protects articular cartilage from fibrillation by functioning as a boundary lubricant and is further concentrated in the damaged surface layer of cartilage in an effort to protect from deeper fibrillation. *We hypothesize that the lubricin boundary layer can be enhanced through gene mediated synthesis, and that a combined effect to limit further malacia can be derived by suppressing the principal degradative cytokine, interleukin 1.* This treatment paradigm builds on the role of interleukin-1 antagonist protein (IL-1Ra) as the gatekeeper for rampant IL-1 induced matrix catabolism, combined with the fundamental knowledge garnered from biophysical and functional lubricin and galectin studies that show lubricin supplementation can enhance boundary lubrication and limit the impact of osteoarthritis. The hypothesis will be tested by several specific aims. 1) Clone and propagate a functional lubricin expression cassette. 2) Determine how cells adhere and migrate along or through the lubricin boundary layer. 3) Develop a combinatorial gene construct co-expressing lubricin and IL-1 receptor antagonist. 4) Evaluate the OA attenuating effects of gene enhanced lubricin synthesis and IL-1 blockade using stem cell vehicles to populate cartilage and synoviocytes by direct injection. Data in rodent models supports the use of lubricin as a gene delivered therapy for the prevention and treatment of post-traumatic osteoarthritis. However, evidence to support the use of lubricin in a larger translational model is lacking. Dual axis therapy, combining gene-based lubricin supplementation with IL-1 receptor antagonist delivery is appealing for controlling OA. The equine carpal fragmentation model will be used, which induces progressive OA without severe lameness. The added novelty of stem cell delivered lubricin and IL-1Ra gene delivery will not only add pluripotent cells to improve cartilage repair but also seed the synovial lining with lubricin secreting cells, to add a dual benefit of enhanced lubrication and IL-1 receptor blockade at both synovial membrane and cartilage interfaces.

**Harry M. Zweig Memorial Fund
for Equine Research - 2016**

P.I.:	Dr. Bettina Wagner
Title:	Effects on equine herpesvirus (EHV) vaccination frequency on host immunity on EHV-1
Project Period:	1/1/16-12/31/16
Reporting Period	1/1/16-12/31/16

TITLE: Effects on Equine Herpesvirus (EHV) Vaccination Frequency on Host Immunity on EHV-1

PRINCIPAL INVESTIGATOR(S): *Bettina Wagner*

Equine herpesvirus type 1 (EHV-1) continues to cause severe outbreaks of abortions or myeloencephalopathy in horses despite widely used vaccination. Current EHV vaccines have decreased abortion storms but neurological EHV outbreaks have continued to occur in recent years. Equine industry and the equine veterinary community have responded with a tendency to increase vaccination frequency. The American Association of Equine Practitioners (AAEP) recommends EHV vaccination every 6 months for competing horses. Some vaccine suppliers recommend vaccinating every 3 months. In addition, equine events may require frequent EHV-1 vaccination with documentation that the horse has been vaccinated within a certain time frame preceding the event (often less than 30 days). However, data to support that frequent administration of EHV vaccines improves immunity and protection from disease are widely missing.

Preliminary data: We have previously vaccinated 15 pregnant mares in short intervals of 60-90 days between vaccinations as currently recommended by the AAEP EHV vaccination guidelines. Because of the EHV-1-free status of our Cornell Icelandic herd, all horses have been monitored monthly for EHV-1-specific antibodies and cellular immunity. ***This revealed a surprising result: Frequent EHV vaccination with an inactivated commercial EHV vaccine resulted in declining antibody values and cellular immunity at several time points after vaccination and immune parameters declined despite additional vaccine boosts.*** This observation is summarized here as ‘***adverse immunity to EHV vaccination***’. Our preliminary data further suggested that adverse immunity occurred more often if vaccine intervals of 60 days were used.

**Harry M. Zweig Memorial Fund
for Equine Research - 2016**

P.I.:	Dr. Gerlinde Van de Walle
Title:	Defining the Relationship between Equine Herpesviruses and Development of the Equine Gastric Ulcer Syndrome (EGUS)
Project Period:	1/1/16-12/31/16
Reporting Period	1/1/16-12/31/16

TITLE: *Defining the Relationship between Equine Herpesviruses and Development of the Equine Gastric Ulcer Syndrome (EGUS)*

PRINCIPAL INVESTIGATOR(S): *Gerlinde Van de Walle*

Although equine gastric ulcer syndrome (EGUS) has a known negative impact on equine performance, only a few options exist to treat gastric ulcers in competitive horses and those treatments are mainly focused on supportive care. Importantly, treatment of EGUS can be expensive and does not address the etiology of this syndrome. Therefore, proper knowledge regarding the causal factors in EGUS development is needed for the development of targeted, more efficacious therapeutics.

Recently, we preliminary demonstrated the presence of EHV-2 and EHV-5, two equine gammaherpesviruses that are correlated with “general malaise” or “poor performance” in racehorses, in a limited set of gastric ulcer samples. These findings have led to our hypothesis that equine herpesvirus infections could play a significant role in the development of the equine gastric ulcer syndrome (EGUS).

In order to test this, we propose two related, but independent aims in this 1-year proposal. In Aim 1, we will characterize the relationship between EHV-2/EHV-5 and the development of gastric ulcers in more detail by studying a large number of gastric tissue samples. These samples will be thoroughly studied on a macroscopic (ulcer distribution and severity), microscopic (immunohistochemistry to detect EHV-2/-5 proteins) and molecular level (PCR to identify EHV-2/-5 DNA). In Aim 2, we explore the efficacy of antivirals and other drugs against equine gammaherpesviruses *in vitro*, using a combination of cytotoxicity assays, plaque assays and quantitative PCR analyses.

Publications:

1. Cossic BGA, Pennington MR, Glaser AL, Van de Walle GR, and Duhamel GE. (2017). Morphological correlation of gammaherpesvirus-5 cellular replication with immune and inflammatory responses in equine multinodular pulmonary fibrosis. *Manuscript in preparation.*
2. Pennington MR, Cossic BGA, Perkins GA, Glaser AL, Duhamel GE, and Van de Walle GR. (2017). The first report of equid herpesviruses 2 and 5 in equine gastric mucosa samples from normal horses and horses with equine gastric ulcer syndrome (EGUS). *Manuscript in preparation.*

APPENDIX B

SUMMARY OF 2016 EXPENDITURES

2016 Research Awards	\$429,242
2017 Public Relations and Administrative Budget	\$28,000
2016 Incentive Awards	\$10,000
Total Expenditures:	<u>\$467,242</u>

APPENDIX C

RESEARCH PRESENTATIONS

November 16, 2016

Cornell College of Veterinary Medicine

Ithaca, New York

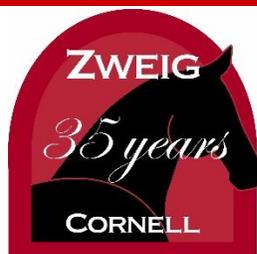
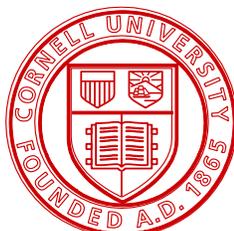
8th Annual Harry M. Zweig Memorial Fund for Equine Research
Poster Session & Talks Cornell College of Veterinary Medicine
Ithaca, New York

FEATURING SPEAKERS FROM CORNELL'S COLLEGE OF VETERINARY MEDICINE

Wednesday, November 16, 2016

Clinical Program Center – C2-537 –

3:00PM Welcome! *Bettina Wagner - Associate Dean Research/Graduate Education*



COLLEGE OF VETERINARY MEDICINE
RESEARCH PRESENTATIONS

Etiology and Prevention of Equine Serum Hepatitis (Theiler's Disease)

Dr. Thomas Divers -- Steffen Professor of Veterinary Medicine, Section Chief;
Section of Large Animal Medicine

<http://www.vet.cornell.edu/faculty/Divers/>

Host Immunity against Equine Herpes Virus 1 (EHV 1) in a Model of Immunologically Naïve Horses

Dr. Bettina Wagner – Associate Dean for Research & Graduate;
Professor of Immunology; Zweig Assistant Professor (2009-2011)

<http://www.vet.cornell.edu/popmed/bios/bettinawagner.cfm>

Preliminary Study of Risk Factors associated with Biaxial Proximal Sesamoid Bone Fractures in Thoroughbred Race Horses

Dr. Scott Palmer -- -- Chief Veterinarian, Animal Health & Diagnostic Laboratory;
New York State Equine Medical Director

<http://www.vet.cornell.edu/news/ScottPalmer.cfm>

Poster Session and Reception - S2-120 Schurman Hall

<http://www.vet.cornell.edu/zweig/>

*Cornell University & Harry M. Zweig Memorial Fund for Equine
Research Presentations - November 16, 2016
Equine researchers present to the Zweig Committee
Cornell College of Veterinary Medicine, Ithaca, New York*



Faculty from Cornell University's College of Veterinary Medicine, Ithaca, New York, and invited speakers, presented a series of equine-related research projects and lectures on November 16, 2016 at the College. The research presentations and poster session were well attended by the committee members of the Harry M. Zweig Memorial Fund for Equine Research, College faculty and staff, and others from around the university.

Speakers included *Thomas Divers* -- Steffen Professor of Veterinary Medicine, Section Chief, Section of Large Animal Medicine, Bettina Wagner – Associate Dean for Research & Graduate Education, Professor of Immunology, Zweig Assistant Professor (2009-2011), Scott Palmer, Chief Veterinarian, Animal Health & Diagnostic Laboratory, New York State Equine Medical Director and their respective lecturers; “Etiology and Prevention of Equine Serum Hepatitis (Theiler’s Disease)”, “*Host Immunity against Equine Herpes Virus (EHV 1) in a Model of Immunologically Naïve Horses*”, “*Preliminary Study of Risk Factors associated with Biaxial Proximal Sesamoid Bone Fractures in Thoroughbred Race Horses*”.

The annual meeting was held on Thursday, November 17, 2016 at the College of Veterinary Medicine, Ithaca, NY, and the committee welcomed Dr. Laura H. Javsicas to her first committee meeting. Dr. Javsicas is board certified by the American College of Veterinary Internal Medicine in Large Animal Medicine and has special interests in neonatology, ultrasonography, cardiology, gastrointestinal diseases and emergency/critical care medicine. Dr. Javsicas joined Rhinebeck Equine in 2013. Dean Lorin Warnick, thanked current and new members for the dedication, expertise and knowledge they bring to the Zweig Committee, which is a big part of the success of the Zweig Fund in helping to support projects related to equine research.

The Harry M. Zweig Memorial Fund for Equine Research honors the late Dr. Harry Zweig, a distinguished veterinarian, and his numerous contributions to the state's equine industry. In 1979, by amendment to the pari-mutuel racing and wagering law, the New York State legislature created the Harry M. Zweig Memorial Fund for Equine Research to promote equine research at the Cornell University College of Veterinary Medicine. The Harry M. Zweig Committee was 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. The Fund contributes a percentage of its revenue to support a variety of equine-related research. The Fund is proud to support the Harry M. Zweig Memorial Fund for Equine Research. This first-rate research helps to provide protection and preventative planning for the equine industry, which in turn helps to ensure a healthy and positive future for the horse racing industry.

The committee administering the fund always includes the chairman of the New York State Racing and Wagering Board or his designee, the dean of the College of Veterinary Medicine at Cornell or his designee, a member or the executive director of the Agriculture and New York State Horse Breeding Development Fund, a member or the executive director of the New York State Thoroughbred Breeding and Development Fund, and at least five New York State breeders, owners, trainers, or veterinarians in equine practice. Dean Lorin Warnick currently serves on the committee, representing the College and its many researchers who have received the Fund's support for research projects advancing equine health and athleticism.

APPENDIX D
AWARDS FOR 2017

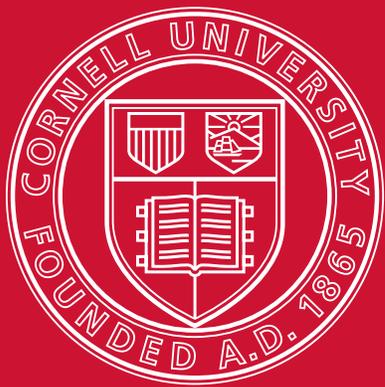
APPENDIX D

2017 Harry M. Zweig Memorial Fund for Equine Research Awards

<u>CONTINUATION</u>		<u>ANNUAL AWARD</u>
Dr. Mohammed	Factors Associated with Musculoskeletal Injuries and Catastrophic Events in Racing Horses (Year 2)	\$75,676
Dr. Wagner	Effects of Equine Herpesvirus (EHV) Vaccination Frequency on Host Immunity to EHV-1 (Year 2)	\$78,993
	Sub-Total:	\$154,669
<u>NEW/Revised</u>		<u>ANNUAL AWARD</u>
Dr. Antczak	Cellular Immunity to Equine Herpesvirus Type 1 (EHV-1) (1 year award)	\$68,410
Dr. Antczak	Functional Gene Annotation in the Horse (2 year award)	\$64,663
Dr. Cheetham	Regenerative Approach to Recurrent laryngeal Neuropathy (2 year award)	\$43,130
Dr. Ducharme	Two-Day Tie-Back (injection Laryngoplasty); Proof of Principle (1 year award)	\$60,000
Dr. Fortier	Does Intra-Articular Stifle Anesthesia Alleviate Lower Limb Lameness? (1 Year award)	\$43,032
Dr. Fubini	The Relationship between obesity and Post-Operative Incisional Infections following Abdominal Surgery in the horse (2 year award)	\$18,120
Dr. Reesink	Quantitative Computed Tomography & Bone Quality Assessment for the Prediction of Fetlock Breakdown Injuries in Racehorses (2 year award)	\$99,180
Dr. Van de Walle	Microencapsulate stem Cells to Promote Wound Healing (2-Year award)	\$53,140
	Sub-Total:	\$449,675
	TOTAL:	\$604,344

APPENDIX E

ZWEIG NEWS CAPSULES



Zweig

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



No. 61 June 2016

Genes influence sarcoids in horses

Sarcoids are the most common form of cancer in horses; the skin tumors develop as small bumps under the skin or scaly lesions that can easily be removed by a veterinarian, but can turn lethal in some horses. Until now, little was known about why the papillomavirus behind sarcoids strikes some horses and passes over others. A new study by an international research group led by scientists at the Baker Institute for Animal Health at Cornell's College of Veterinary Medicine reveals that genetic differences in immune function between horses partly accounts for these differences. The results could eventually help scientists design a therapeutic vaccine for sarcoids that could be administered to horses to help their immune systems fight off the infection.

"Many therapies have been proposed as the 'best' treatment for sarcoids," says Doug Antczak, the Dorothy Havemeyer McConville professor of equine medicine who led the study. In some horses, tumors develop as small bumps under the skin or scaly lesions that can easily be removed by a veterinarian, but in other horses the problem becomes much more serious. Surgery, cryotherapy (freezing the tissue), laser treatment, injecting the tumors with drugs to kill the cells, radiation treatment, and immunotherapy have all been shown to cure these more recalcitrant tumors, "but some tumors tend to recur no matter what treatment is used, and there is no universal consensus on a uniformly successful therapy," says Antczak.

Antczak says scientists have known for years that bovine papilloma-virus (BPV) is the most likely culprit behind sarcoid tumors. Recent work from Europe suggests that variants of this virus have become adapted to horses and are probably the cause of most sarcoids.

Antczak and his team used a genome-wide association study to compare the genetic makeup of horses with and without sarcoid tumors at over 50,000 sites in the equine genome. They studied 82 sarcoid-bearing horses from the US and United Kingdom and 272 controls that did not have sarcoids. They found regions



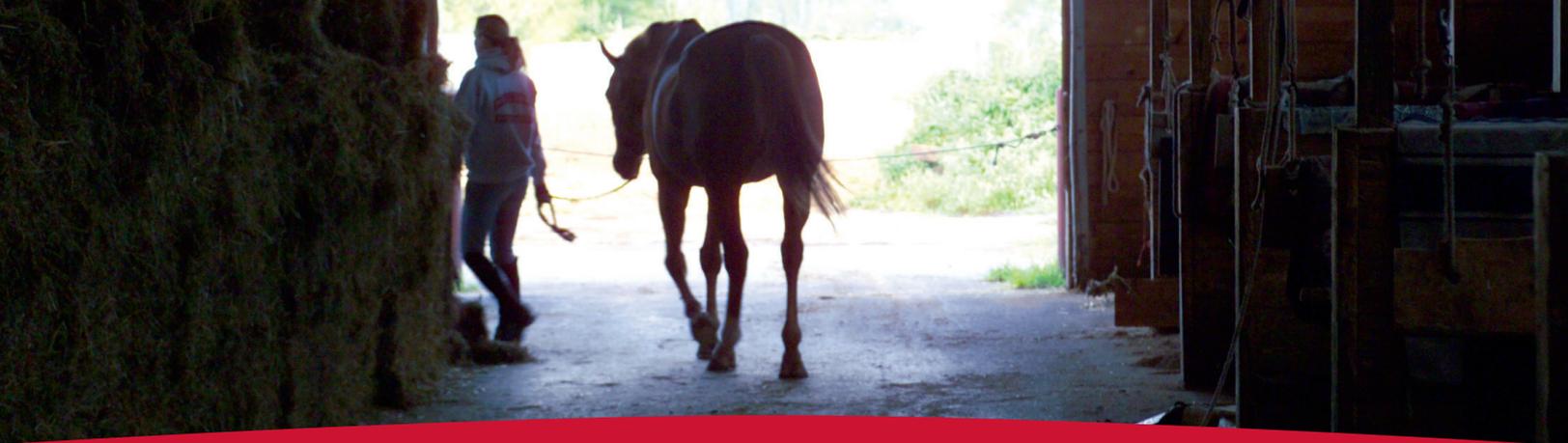
Dr. Doug Antczak

on chromosomes 20 and 22 that tended to be different in horses diagnosed with sarcoids, hard evidence that a horse's genes determine, in part, how susceptible it is to sarcoids.

Interestingly, this genetic link implicates the immune system in sarcoid susceptibility. The region of chromosome 20 associated with sarcoid development is located within a portion of the genome responsible for immune function called the Major Histocompatibility Complex (MHC) class II region. The MHC type that is associated with sarcoid susceptibility is very rare among Standardbred horses, a fact that may explain why sarcoid is diagnosed so rarely in this breed.

Antczak says knowing that the virus takes advantage of horses with a particular immune feature means a therapeutic vaccine for sarcoids could eventually be developed to bolster the immune response and help a horse recover.

Once such a vaccine is developed, "you could identify horses that are genetically susceptible and vaccinate them, or wait and treat them with the vaccine once they develop sarcoids," says Antczak.



Harry M. Zweig Memorial Fund For Equine Research 2016 Awards

NEW

\$58,702 to Dr. Julia Felipe for "Reducing Equine Herpes Virus Viral Load & Recurrence through Epigenetic Control"

\$63,887 to Dr. Lisa Fortier for "Macrophage Regulation of Mesenchymal Stem Cell Function in Tissue Regeneration"

\$72,661 to Dr. Hussni Mohammed for "Factors Predisposed to Musculoskeletal Injuries and Catastrophic Events in Racing Horses"

\$100,000 to Dr. Alan Nixon for "Arthritis Control through Dual Axis Lubricin Over-Expression and Catabolic Cytokine Antagonism"

\$84,750 to Dr. Bettina Wagner for "Effects of Equine Herpesvirus (EHV) Vaccination Frequency on Host Immunity to EHV-1"

\$49,242 to Dr. Gerlinde Van de Walle for "Defining the Relationship between Equine Herpesvirus & Development of the Equine Gastric Ulcer Syndrome (EGUS)"

CONTINUED

\$50,250 to Dr. Robert Gilbert for "Controlled Postponement of Ovulation in Mares"

\$62,715 to Dr. Alan Nixon for "Enhanced Breakdown Screening in Thoroughbred Racehorses through Multimodal Imaging & Serum Biomarker Combinations"

\$82,514 to Dr. Tracy Stokol for "Platelets are a Trojan Horse that Deliver Equine Herpes Virus to Endothelial Cells"



Zweig Memorial Trot 2016

Vernon Downs, Vernon, N.Y.

Sunday, July 24, 2016

Post Time: 6:45 PM

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

Trooping the colour: an invitation to the Queen's 90th birthday celebration



By Pat Wehle, Harry M. Zweig Memorial Fund Committee member

As a lifelong horseman and admitted “Royal Nerd,” I was thrilled to receive an invitation to attend the Queen’s 90th Birthday Party at Windsor Castle in May. The program was a salute to the Queen from the Commonwealth including 900 horses and 1500 people. It turned out to be truly the trip of a lifetime.

I received the invite to attend thanks to my involvement with a wounded veterans’ program at the Equicenter in Mendon, NY. We provide therapeutic riding for wounded military and their families. There is a high incidence of suicide among our veterans, and therapeutic horseback riding has been shown to make a huge positive difference to veterans’ mental health to the point of preventing potential suicides. I’m thrilled to support this program. Several years ago, we developed a relationship with the Queen’s Household Cavalry Guards, the Queen’s personal bodyguards. Founded in 1660, it’s arguably the most prestigious military unit in the world. Last fall four of the Guardsmen came to visit the Equicenter to see first-hand how our program worked and to meet our veterans. We are eager to share best practices and procedures with anyone interested in the welfare of wounded veterans. The

invitation to the birthday party came through the Household Cavalry Guards Foundation.

To say this was the quintessential example of British Pomp and Circumstance, is an understatement. Horses and bands from Oman, Azerbaijan, Canada, and Fiji among others were featured. The best and most moving performances were I think, the Household Cavalry Musical Ride and the King’s Troop Royal Horse Artillery Musical Drive. It was astounding.

Our group was invited to tour the Knightsbridge Barracks the next day, and also visited the Horse Trust, which accepts retired police horses, some of the Queen’s horses, and rescues horses from the region. They are one of the largest funders of equine research in Europe and may provide opportunities for collaborative research work.

It was truly and extraordinary experience. Above all, we hope this relationship will help us spread the word about dramatic positive effects therapeutic riding has on the health and well-being of our wounded veterans and their families.

Above Left: Patricia Wehle and veterinarian for the Household Cavalry Guards. Above Right: Mercury, a Drum Horse in the Queen’s Band of the Life Guards.

To save paper by receiving electronic copies of this newsletter, email lam78@cornell.edu with “subscribe Zweig newsletter” in the subject line or download at <http://bit.ly/ZweigNews>

Still in step

by Teresa Genaro

Zweig Committee Member Bill Wilmot and his wife Joan Taylor were profiled in the March 2016 issue of the New York Thoroughbred Breeder's magazine, discussing their work on Stepwise Farm, their career paths as veterinarians and breeders, and their experiences in running a small, but successful business.

Below is an excerpt from the profile piece. Please visit <http://www.nytbreeders.org/magazine> to read the full story.

Though they've downsized their commercial breeding business, both Wilmot and Taylor remain active in the industry. He serves on the board of the New York State Thoroughbred Breeders' Development Fund; she was elected to the board of New York Thoroughbred Breeders after being appointed last year to fill the spot vacated by Barry Ostrager, who resigned after being appointed to the Civil Branch of the New York state Supreme Court.

Taylor is also designing a series of educational seminars for the state's breeders.

"It's a nice way to help give back to the industry," she said. "We've got some very experienced people in the state, and this is an opportunity for them to share their knowledge."

Sponsored by the Breeders' Development Fund and NYTB, the first seminar, on foaling mares, was held in December at Fasig-Tipton's Humphrey S. Finney sales pavilion in Saratoga Springs. The next is scheduled for April 30 and will focus on raising horses from foals to yearlings.

"We try to do timely topics related to what's going on in the breeding industry at that time of year," Taylor explained. "The first one was very well attended."

With decades of success as commercial breeders behind them, Taylor and Wilmot know what it takes to breed and raise a foal that will sell well, but it's that experience that has tended to keep them humble.

"You always need luck," said Taylor. "You can't ever think you know it all. You can do everything right and things still don't work out. It's an unbelievable gauntlet, from the time you make the decision to breed a mare to picking the stallion to when the hammer falls. It's always great when your horse goes to the sale looking great and has learned to walk and behaves and is well-received. It's rewarding for the whole staff."

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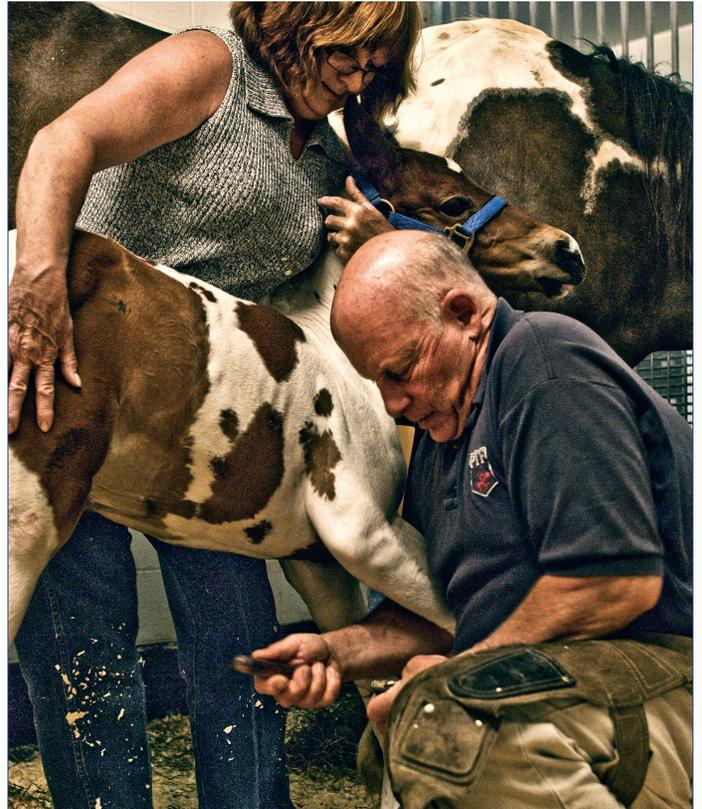


Bill Wilmot and Joan Taylor
Photo credit: Skip Dickstein

Hall of Fame farrier

Cornell Head Farrier Steve Kraus was inducted into the International Horseshoeing Hall Of Fame in Louisville, Kentucky on February 4, 2016. The hall honors farriers around the world who have made significant contributions to the profession. Nominations are submitted by peers, trainers, veterinarians, horse owners, friends and family members, and winners are chosen by current hall members.

Kraus first began horseshoeing as an undergraduate at Cornell, and eventually became head of the Cornell Farrier Program. In this role, Kraus teaches his students the theory behind basic and corrective horse shoeing and hoof trimming; therapeutic methods; splint fabrication and more, followed by hands-on practice under his supervision. He travels and lectures about horseshoeing topics nationwide. Kraus also runs an annual Farrier Conference, now in its 32nd year. Professionals from across the U.S. attend to learn the latest techniques as well as the time-honored crafts of blacksmithing and tool making, taught by experts.



Head Farrier Steve Kraus tends to a foal's hooves.

Cornell Ruffian Equine Specialists using 4DDI robotic scanners to produce real-time 3-D images

Cornell Ruffian Equine Specialists (CRES), an affiliate of the College of Veterinary Medicine at Cornell University, has acquired one of the world's first open-format standing computed tomography (CT) scanners. The EQUIMAGINE™ system, developed by Four Dimensional Digital Imaging (4DDI), uses two or four computer-controlled robots to maneuver around the horse's body. It produces three-dimensional, real-time images that permit equine surgeons to precisely evaluate the structure of the animal's limbs, head, neck and in the near future, torso.

"The quality and resolution of the real-time images created with the 4DDI system far exceed those of existing technology," says CRES Clinical Director Tom Yarbrough. "It represents a giant leap forward in our ability to detect problems at the earliest stages, when they are far easier and less expensive to address."

Existing CT systems require that the horse be anesthetized and lying down. Horses scanned by the 4DDI system are sedated and standing, avoiding the risks associated with anesthesia and prolonged recumbency.

And while existing CTs are limited to the parts of the animal that fit into the cylindrical machines, the new system facilitates an unlimited range of motion and unencumbered access to the horse's entire anatomy. Yarbrough says CRES is now working with 4DDI to integrate a treadmill with the system for motion analysis. CRES surgeons also will use the 4DDI system for preoperative planning and evaluation of complex fracture reconstructions during surgery, as well as rapid evaluation of skull and sinus disease.

Racing continuing education modules reins in thoroughbred fatality rates

Horse racing fatalities are a serious issue being investigated by Zweig-funded researchers. A direct result of this effort is a brand-new continuing education (CE) module titled "Introduction to Thoroughbred Risk and Protective Factors," now available on the Grayson-Jockey Club Welfare and Safety of the Racehorse Summit Website (<http://courses.grayson-jockeyclub.org>).

The module caps of more than a year of collaborative effort between author Dr. Scott Palmer, equine medical director of the New York State Gaming Commission, and Alicia Benben,

academic coordinator and instructor at BCTC-NARA (Bluegrass Community and Technical College-North American Racing Academy).

Data presented in the module represents information obtained from the NYSGC-Cornell University Post Mortem Examination Program and the epidemiological research funded by the Zweig Committee.



Dr. Scott Palmer

"One of the most important aspects of the epidemiological and pathological research we are doing is that we are not just writing scientific manuscripts," says Palmer. "We are bringing this information directly to the horse trainers and veterinarians in a very practical format so that they can help prevent injuries in the future."

According to Palmer, this work has thus far resulted in a 50% decrease in Thoroughbred racing fatalities in the past four years. Prior to starting this program, the thoroughbred fatality rate in New York was 2.1/1000 starts. In 2014, that rate was reduced to 1.3/1000 starts, and in 2015 it was 1.4/1000 starts. In the first six months of 2016, the thoroughbred fatality rate was 1.1/1000 starts. "The referenced CE Module is part of that effort," says Palmer.

This is the fourth course to be offered as part of a Grayson-Jockey Club CE initiative that originated with the Grayson-Jockey Club Welfare and Safety Summit in 2015. These interactive courses are free and can be used for credit for the proposed New York Required CE program for trainer continuing education.



In case you missed it:

Lecture Schedule at 7th Annual Harry M. Zweig Memorial Fund for Equine Research Poster Session & Talks:

- Interleukin-10 Overexpression helps Protect Equine Cartilage in Osteoarthritic Model (Kyla Ortved – Assistant Clinical Professor)
- Early Response of the Equine Corpus Luteum to Pregnancy (Robert Gilbert – Professor)
- The Equine Mesenchymal Stem Cell Secretome as a Novel Therapy in Wound Healing (Gerlinde Van de Walle - Assistant Professor)
- Current Concerns in the Horse Industry (Dr. Ann Dwyer—2013 President of AAEP)
- Immunomodulation to Improve Peripheral Nerve Regeneration (Joy Tomlinson – Cornell Clinical Fellow)

Dr. Hélène Marquis seeks safer strangles vaccine

Strangles, an illness caused by the bacterium *Streptococcus equi*, affects the upper respiratory tract of horses, can last for several weeks and cause serious and long lasting respiratory problems. The disease is highly contagious and outbreaks are difficult to control because a large number of affected horses become carriers. Although the vaccines that are currently available confer moderate protection, they occasionally induce abscess formation and carry a risk of exacerbating the infection.



Through funding from the Zweig Fund, Dr. Hélène Marquis, professor of microbiology and immunology at Cornell, is studying the molecular mechanisms of pathogenicity of *S. equi* and planning to create a safe and protective vaccine against strangles. "One of the major hallmarks of *S. equi* pathogenesis is its ability to resist killing by neutrophils," says Marquis. "Although neutrophils [white blood cells] migrate in large numbers to the site of infection, their ability to phagocytose [consume] and kill *S. equi* is highly compromised."

Marquis says this phenomenon is due in part to *S. equi* having an outer capsule with strong anti-phagocytic and non-immunogenic properties. *S. equi* also possess long hair-like appendages on its surface, known as pili. "We hypothesize that these pili contribute to the ability of *S. equi* to colonize tissues" says Marquis, "and that anti-pilus antibodies can neutralize the anti-phagocytic activity of the capsule and consequently increase the ability of the host's immune system to then kill the bacteria."

To test this hypothesis, Marquis' team will purify pili to generate anti-pilus antibodies, and then test to see if they will increase the efficacy of the host's immune response to the bacteria.

"If the results support our hypothesis, it will imply that elicitation of anti-pilus antibodies in the horse may confer protection against strangles by two mechanisms," says Marquis. "One, by increasing the efficacy of neutrophil and complement-mediated killing of *S. equi*, and two, by compromising the attachment of *S. equi* to tissues."

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.

CORNELL UNIVERSITY COLLEGE OF VETERINARY MEDICINE 2016 HARRY M. ZWEIF MEMORIAL FUND COMMITTEE

Scott Ahlschwede, DVM
*Rood & Riddle Equine Hospital
Saratoga Springs, N.Y.*

Gabriel Cook, DVM
*New England Equine Practice
Patterson, N.Y.*

Janet Durso, DVM
Middletown, N.Y.

Ann Dwyer, DVM
*Genesee Valley Equine Clinic, LLC
Sottsville, N.Y.*

Laura Javicas, VMD
*Rhinebeck Equine LLP
Rhinebeck, N.Y.*

Paul C. Mountan, DVM
*Rhinebeck Equine LLP
Rhinebeck, N.Y.*

Ron Ochrym
*Director Division of Horseracing
NYS Gaming Commission
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Cornell University College of Veterinary Medicine*

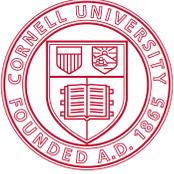
Patricia Wehle
Fairport, NY

Robert Williams
*Executive Director New York State Gaming Commission
Schenectady, N.Y.*

William Wilmot, DVM
Saratoga Springs, N.Y.

Brian Zweig
Rensselaer, N.Y.





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Welcome to our new Zweig Committee members



Scott Ahlschwede, DVM

*Rood & Riddle Equine Hospital
Saratoga Springs*

Dr. Scott Ahlschwede graduated from Texas A&M College of Veterinary Medicine and began his veterinary career in Lexington, Kentucky as an intern at Rood & Riddle Equine Hospital in 1996. He practiced in the Lexington area for 15 years as an ambulatory veterinarian specializing in reproduction, primary and preventative care, and sales evaluation. In 2012, Ahlschwede moved to upstate New York to develop Rood and Riddle's first practice outside of Lexington, Kentucky.



Laura Javsicas, VMD

Rhinebeck Equine LLP Rhinebeck, NY

Dr. Laura Javsicas received a B.A. in Biology from Cornell University, where she was co-captain of the equestrian team, then attended veterinary school at the University of Pennsylvania. After receiving her VMD in 2004,

she did a one-year internship at the Hagyard Equine Medical Institute in Lexington, Kentucky. Javsicas then completed a three-year residency in equine internal medicine at the University of Florida. Following her residency, she stayed on at the University of Florida as a member of the faculty. In 2009, she moved to Saratoga Springs, where she worked at an equine clinic providing in-hospital internal medicine services and general ambulatory care until joining Rhinebeck Equine in 2013. Javsicas is board certified by the American College of Veterinary Internal Medicine in Large Animal Medicine and has special interests in neonatology, ultrasonography, cardiology, gastrointestinal diseases and emergency/critical care medicine.

And, a very heartfelt thanks to our outgoing Zweig Committee members:

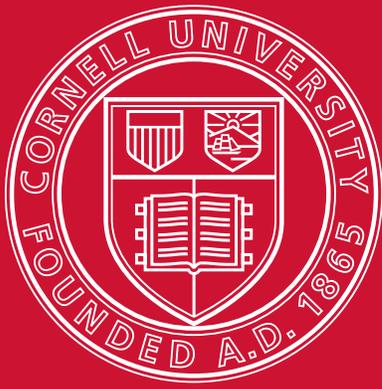
- Jean Brown – Sr. Vice President Operations – Blue Chip Farms, Inc.
- Paul Kelley - Kelley Racing Stable, LLC

Have you visited our Web site lately?

www.vet.cornell.edu/research/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.



Zweig

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



No. 62 October 2016

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."

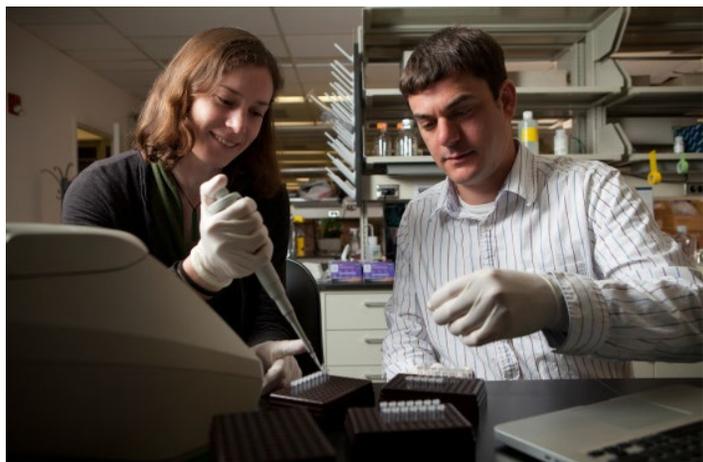
Felipe studied veterinary medicine at Universidade Estadual Paulista in Botucatu, Brazil. After a few years practicing in horse breeding farms and evaluating (and riding) endurance horses, she traveled to Kansas State University College of Veterinary Medicine, where she completed an internship in equine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