



# Grayson-Jockey Club

# RESEARCH TODAY

The Newsletter for Benefactors of Grayson-Jockey Club Research Foundation, Inc.

## RECORD \$1.2 MILLION IN EQUINE RESEARCH IN 2008

Grayson-Jockey Club Research Foundation's board of directors has approved a record allocation of \$1,226,457 for equine research in 2008. The funds will underwrite a slate of 14 start-up projects and 10 second-year proposals.

This marks the foundation's fourth consecutive year of record funding and the second consecutive year that it is providing more than \$1 million for equine research.

This year's slate of projects brings the foundation's totals during the last 25 years to more than \$15.5 million for 239 projects at 35 institutions.

In addition to funding the 12 new grants described below, the foundation set aside funds for special projects on racetrack surface management and the effects of various surgical procedures to correct limb deformities in young foals. Both of these subjects are among key considerations in the industry's ability to protect the soundness and safety of racehorses.

### ***NEW PROJECTS***

#### **HYDROCORTISONE REPLACEMENT THERAPY IN SEPTIC FOALS**

*Dr. Michelle Henry Barton, University of Georgia*

Infection is regarded as the number one cause for illness and death in newborn foals. This research team — involving scientists at the univer-

sities of Georgia and Florida as well as Cornell University — reports that about 75% of newborn foals admitted to referral hospitals have the condition, and at least 25% of those are lost. Production of the hormone cortisol is a defense against infection, but perhaps as many as 50% of infected newborns (septic foals) suffer from insufficiency of cortisol. A synthetic cortisol product, hydrocortisone, is used in human medicine to reduce incidence of death in such cases. This project will seek to determine a safe dose of hydrocortisone that will reduce severity of disease and improve survival rates of septic foals, in a controlled hospital setting.

#### **DOES AIRBORNE EXPOSURE PREDICT PNEUMONIA?**

*Dr. Noah Cohen, Texas A & M*

The foundation has funded several projects on viral pneumonia, a major cause of death in foals. There is no effective vaccine, and among questions unanswered are why some farms experience a higher incidence than others and why some foals on a given farm become infected while others do not. This project is a continuation of research by one of the leading epidemiologists in North America. (It was Dr. Cohen whom the foundation called on to head the epidemiologic team when it partnered with the Commonwealth of Kentucky in an initial study on

MRLS.) In this present proposal, Dr. Cohen will test whether existence of virulent R. equi in the air predicts the outset of the disease. If the answer is positive, farms could initiate strategies to reduce the amount of contamination.

#### **MAPPING OCCLUSION OF VEINS IN EIPH**

*Dr. Fred Derksen, Michigan State University*

This is another approach in the series of attempts to understand fully why so many horses experience bleeding (Exercise Induced Pulmonary Hemorrhage: EIPH) in the lungs as a result of high exercise. In past research funded by the foundation, this research team discovered scarring around blood vessels, which obstructs the veins and causes back-up in the lungs and rupture of its small blood vessels. This new project is designed to determine the location and extent of vein scarring in the lungs and compare it to horses that have not raced, also relating the location of the scarring with the location of the bleeding. Another aspect will be investigating why vein scarring occurs by studying molecules in the vein walls that signal scarring to occur. This project has the potential to guide research in a new direction for effective prevention and/or treatment of a widespread occurrence.

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is the newsletter of

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a 501(c)(3) organization

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## RECORD FUNDING *(continued from page 1)*

### **DIFFERENTIATION OF STEM CELLS FOR CARTILAGE REPAIR**

*Dr. Alan Nixon, Cornell University*

Cartilage damage affects both yearlings and horses in training and commonly triggers the development of arthritis. The resultant stress of the joint also can lead to fractures of the pastern or cannon bone. Dr. Nixon points out that “despite popular perception, cultured stem cells or marrow-derived mixtures so far seem incapable of forming durable cartilage.” Past attempts have created only transitory effects on cartilage. His current approach is to utilize and test robust gene-based methods to turn stem cells from the animal’s own marrow into dedicated cartilage cells: “These equine specific genes have been recombined into non-viral vectors that insert them into the chromosomal DNA of target cells.”

### **EFFECTS OF COMBINING LIDOCAINE AND FLUNIXIN**

*Dr. Butch KuKanich, Kansas State University*

This grant examines the dosages of lidocaine and flunixin to ensure safety of the animals being treated. The two medications are often used together, especially after surgery for colic and other intestinal problems. Lidocaine has narrow parameters for dosages and can create toxicity, which results in seizure and collapse — putting the horse, and its handlers, in danger. The study will seek to determine if commonly used dosages need to be adjusted because of how these drugs interact.

### **A RESPIRATORY MODEL ON INTERACTIONS OF VIRUS AND HOST**

*Dr. Gisela Sobol, Colorado State University*

Dr. Sobol points out that “despite years of research, major epidemics of EIV and EHV-1 remain a world-

wide problem.” This project seeks understanding of why initial encounters of a pathogen determine downstream events and the outcome of the disease. Little is known about that initial situation. This project will employ a specific equine cell culture system to study the initial defense mechanisms in order to develop the necessary knowledge that can lead to immune modulators and anti-inflammatory drugs.

### **XENOGRAFTING TO STUDY TESTICULAR FUNCTION IN STALLIONS**

*Drs. Ina Dobrinski and Regina Turner, University of Pennsylvania*

“Age-related testicular degeneration is a common cause of progressive infertility,” the researchers point out. Underlying causes are not well understood, so no satisfactory treatment has been developed. These researchers found in 2006 that in severe cases it is the testis itself and not the extratesticular environment that is defective. A process known as xenografting will further verify that finding and will also test whether common treatments for testicular degeneration actually have a positive effect on the diseased tissue. Xenografting “will allow us to answer these questions . . . without having to perform experiments on the horses.” Improved understanding could lead to creation and evaluation of more effective treatments for the disease.

### **MOLECULAR EPIDEMIOLOGY OF THE 2006 OUTBREAK OF EVA**

*Dr. Udeni Balasuriya, University of Kentucky*

Since the University of Kentucky is a designated reference lab for the World Organization of Animal Health, many tissue and serum samples from the 10-state outbreak of Equine Viral Arteritis (EVA) of 2006-07 are available there for

research. This project will characterize the genes that encode structural protein of the virus and sequence the genome of EVA samples from different states involved in the outbreak. Because the samples were collected over nearly a year, the evolution of the EVA virus over a period of time can be studied. The researchers should be able to identify “mutational hot spots” and “hopefully have a greater understanding of the genetic basis of persistent EVA infection in the carrier stallion.” The researchers are confident their work will “impact the nature of control measure to prevent EVA infection . . . as well as allow us to develop more reliable molecular diagnostic tests.”

#### **NEUROPATHOGENESIS OF EHV-1 INFECTION**

*Dr. Lutz S. Goehring, Colorado State University*

The foundation has been funding research on the sometimes deadly equine herpesvirus-1 infection for a number of years and last year launched two projects chosen as a result of a special call for research on that subject. The Research Advisory Committee scored this project very highly as a worthy addition to work being done on the subject. Currently there is no effective vaccine, and in fact, there are indications that the vaccines in use might actually be detrimental to horses suffering from the particular type of herpesvirus (EHV-1). The non-existence of experimental models has hampered research. As a solution, these researchers “propose to establish an endothelial cell culture system and . . . to study how the process of virus transfer from white blood cells into endothelial cells occur.” They will also seek methods to intervene with the various processes involved in a horse developing EHV-1.

#### **MOLECULAR AND CELLULAR LEVEL STUDIES OF LAMINITIS**

*Dr. Hannah Galantino-Homer, University of Pennsylvania*

This project takes an approach to laminitis that is aimed, the researchers explain, “to further our understanding by focusing our efforts at the molecular and cellular level.” Currently, laminitis still is so baffling to scientists that researchers tend to be split into two camps (theories) as to cause of the problem — vascular and enzymatic. “The lack of agreement about the basic pathophysiology of laminitis explains why standard guidelines for therapy are not yet available,” noted Dr. Galantino-Homer. If this project can identify which specific genes and proteins are up-regulated or down-regulated during the first phase of the disease — when identifiable symptoms are not yet manifested — it “will determine the pathways of the disease and allow institution of preventive or interventional treatments sooner.” The first phase of laminitis, the developmental phase, is followed, of course, by the acute phase, and one of the frustrations of dealing with the disease is that often by the time it is diagnosed, the horse may be gravely threatened. These researchers believe the study “will provide information that we and other investigators can use to verify or elaborate on existing theories about laminitis, explore previously unrecognized cellular and molecular events during laminitis, and validate in vitro models of laminitis.” The latter will facilitate research projects that do not require laminitic horses.

#### **MECHANISMS OF MAINTENANCE OF EARLY PREGNANCY**

*Guelph University - Dr. Keith Betteridge*

This project addresses the frequent scenario of a mare being diagnosed as pregnant soon after breeding, but quickly losing the pregnancy.

The three-week stage has been identified as the point when the conceptus (embryo and associated tissues and fluids) has to become immobilized at the position in the uterus where the placenta will develop. The research is aimed at understanding the processes by which this either occurs, and the pregnancy continues, or fails to occur successfully. This research team utilizes various physiologic, biochemical, proteomic, and molecular methods to identify changes in proteins, steroid hormones, and other molecules that are altered during the critical phase: “Several distinct differences between normal and failing pregnancies have already” been identified. Continuing understanding from this project could lead to diagnostic tests of the reproductive health of mares as well as treatments that improve the success rate of early pregnancies.

#### **CORD BLOOD STEM CELLS: FROM FARM TO POINT OF CARE**

*Dr. Dean Betts, Guelph University*

This is another project seeking to overcome the problem of stem cells being unsuccessful so far as antidote to cartilage lesions. Research in human medicine indicates that umbilical cord cells are more effective than stems cells from fat or bone marrow. The researchers have already isolated umbilical cord blood stem cells in horses and have “demonstrated their potential to form bone, cartilage, and fat in petri dishes.” This project will continue the learning curve, not only in use of cord stem cells in the horse from which they were harvested, but also allogenic stem cell therapies (use in horses other than the donor). As stated by Dr. Betts, “This knowledge has the potential to greatly enhance clinicians’ ability to make rational decisions regarding the choice of stem cell to use in specific situations.”

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**CONTINUING PROJECTS**

**Levothyroxine as a treatment for insulin resistance in horses (toward a defense against laminitis)**

Nicholas Frank, University of Tennessee; Ray Boston, University of Pennsylvania

**Reducing wound infections of orthopedic surgeries**

Dean Richardson, Thomas Schaer, Noreen Hickok, Christopher Adams. University of Pennsylvania & Thomas Jefferson University

**Control of Rhodococcus equi pneumonia using gallium**

Keith Chaffin, Noah Cohen, Ronald Martens. Texas A& M University

**Blood supply to the mare's uterus is related to infertility: evaluation and treatment**

Irwin Liu, Eugene Steffey. University of California-Davis

**Promoting specific immunity in foals**

D.W. Horohov, C. Merant, C. Breathnach. University of Kentucky

**Normal and abnormal functions of specific proteins in stallion semen**

M.H.T. Troedsson, W.C. Buhi, J.P. Verstegen, M.L. MacPherson. University of Florida

**Calcium/magnesium and hormones in septic foals**

R.E. Toribio, C. Kohn, S. Hurcombe, Nathan Slovis. The Ohio State University and Hagyard-Davidson-McGee, Lexington, Ky.

**The changing shape of the fetlock joint and its important to incidence of joint disease and injury**

Chris Kawcak, C. Puttlitz, C.W. McIlwraith, K. Parkin, K. Morgan. Colorado State University, Animal Health Trust, Newmarket, England, and University of Liverpool

**Efficacy of valacyclovir against neuropathogenic EHV-1**

Lara Maxwell, Oklahoma State University -PI Brad Bentz, Richard Eberle, Charles MacAllister and Jerry Ritche - Associate PIs

**The neurologic EHV-1 marker: correlation or causation?**

Nikolaus Osterrieder, Cornell University



**Rokeby Circle Members**

In honor of the generosity to the Foundation by the late Paul Mellon, Grayson-Jockey Club designates inclusion in the Rokeby Circle for those donors/members at the \$10,000-plus level within the year. The honor is named for Rokeby Farm, Mr. Mellon's estate in Virginia. Current members of the Rokeby Circle as of February, 2008.

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