



Grayson-Jockey Club

RESEARCH TODAY

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

15 NEW PROJECTS FUNDED IN 2010

The directors of Grayson-Jockey Club Research Foundation have approved 15 new projects and four second-year projects for funding in 2010. The projects include two which are being underwritten for \$97,431 by NTRA Charities' fund memorializing Barbaro. They are identified below. The combined total for funding in 2010 is \$889,697. Since 1983, the Foundation individually has provided more than \$17.1 million to fund 270 projects at three dozen universities.

In addition, a separate award, the Storm Cat Career Development Award, is a \$15,000 grant to Catherine Radcliffe of Cornell University.

Following are descriptions of the projects being launched this year:

Race Surface Optimization for Fetlock Injury Prevention (II)

Drs. Sue Stover & Mont Hubbard,
University of California-Davis

This is the logical extension of a one-year grant funded last year in which the use of a 4 X 4 foot box was utilized to duplicate the make-up of race track surfaces. The question of the first project was whether this process could be validated, and early indications are that it was a success. The next step continues the process. The composite review from the Research Advisory Committee included the comment that continuing along this path could eventually

“allow evaluation of literally hundreds of racetrack surface characteristics to better optimize their material properties.”

Ethyl Pyruvate and Endotoxemia in Horses

Dr. Sue Holcombe,
Michigan State University

Endotoxemia is a common cause of death in serious equine conditions such as colitis, strangulating intestinal obstructions, and septicemia. Available treatments are not consistently successful, and finding a clinically useful treatment, without side effects, remains an important goal. That is the basis for this project, which will test whether ethyl pyruvate is a useful medication. It has been shown to ameliorate intestinal, cardiac, and other conditions in humans and other species. In humans, it has been found to be effective in critical illness even after the problem has become acute. Further, it has already been shown to be safe for horses. The investigator hopes to demonstrate that ethyl pyruvate treatment will be more effective than flunixin meglumine, and it would also be considerably less expensive.

In Vivo Gene Transfer for the Treatment of Laminitis

Dr. Dean Richardson,
University of Pennsylvania

Funded through NTRA Charities:
This project seeks to develop a gene

therapy approach to prevent laminitis in the contralateral hoof when a horse is being treated for a musculoskeletal injury. This, of course, was what eventually ended the efforts to save Barbaro and is a frequent threat to horses with hoof and leg injuries. The well known research team already has compelling preliminary data which encourages the hypothesis that use of recombinant adeno-associated viruses can be used as vectors to deliver a therapeutic gene (TMP-3) to the lamellar tissues. This is meant to inhibit the damage to the epidermal laminae without disrupting the normal hoof structure.

Factors Associated with Success and Failure of Early Pregnancy

Dr. Keith Betteridge,
University of Guelph

Pregnancy loss during the third week of gestation is a major problem in horses. Reviewers regarded it likely that this project will provide greater understanding of the interaction of the conceptus and the endometrium at that time of gestation. The probable understanding of proteins associated with early pregnancy loss will help in understanding mechanisms involved in both successful and failed pregnancies, and suggest possible methods of therapy. The techniques employed will include comparison of the transcriptomes of endometrium and trophoblast in successful and unsuccessful pregnancies,

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a 501(c)(3) organization

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characterizing the influences of prostaglandin, and identifying factors produced by the fetus that correlate with the processes of its immobilization. The researchers will examine gene expression of associated proteins, etc., in normal and failed pregnancies to search for markers of early embryonic loss.

Mechanisms of Pulmonary Vein Remodeling in EIPH

Dr. Fred Derksen,
Michigan State University

This is the next step in a sequence of projects undertaken by Dr. Derksen, some funded by the Foundation. This research team has discovered scarring around blood vessels in the lungs of horses affected with Exercise Induced Pulmonary Hemorrhage (EIPH). It is believed that the scarring obstructs the veins, causing blood to back up in the lung and rupture its fragile small blood vessels. The main goal of this next study is to determine why the scarring occurs, by studying changes in molecules in vein walls that occur in response to exercise, both in non-EIPH horses and EIPH horses. Understanding EIPH pathology in general and the vein scarring in particular is described as necessary before the ultimate goal of prevention or more effective treatment could be achieved.

Systemic Effects of Analgesic Combinations in Horses

Dr. Chris Sanchez,
University of Florida

Management of pain is a key element in veterinary care of horses, especially those with colic or lameness. In addition to the humane urge to protect the animal from pain, there is a case management element in that the pain is often accompanied by severe inflammation that can lead to organ failure and founder. Many pain killers, however, have negative side effects including stomach ulcers, diarrhea, and kidney failure, so that

seeking better pain killers is an important subject for research. This project will test lidocaine, ketamine, and butorphanol, individually, and in combinations. The study is predicated on the belief that no ill effects will be manifested.

Rapid PCR Diagnosis of Equine Botulism Types A, B, and C

Dr. Raymond Sweeney,
University of Pennsylvania

Botulism occurs throughout North America and can spread quickly. Last year, one outbreak caused the death of 100 horses. One of the difficulties in managing botulism outbreaks is that the traditional diagnostic test requires two to three weeks. The goal here is to develop a test that can verify the disease much more rapidly. This work will continue that research team's effort previously funded by GJRF. The research capitalizes on recent progress in detection of botulism in humans, driven by the disease's potential as a bioterrorism threat.

Clinical Administration of Doxycycline for Arthritis

Dr. Lisa Fortier,
Cornell University

Treatments for arthritis, a common problem for horses, are divided between those that alleviate pain and those that preserve joint cartilage. There is need for additional, easily administered oral treatments to halt the progression of arthritis. Doxycycline is believed to have potential in alleviating arthritis because it is a potent inhibitor of enzymes called matrix metalloproteinases (MMPs). MMPs are responsible for degrading cartilage in joints, leading to arthritis. One aspect of this study will be to determine a minimal dosing level to treat arthritis, one that is not antibacterial and thus would have no potential for contributing to

drug-resistant bacteria. It is anticipated that if doxycycline is verified as useful treatment against arthritis, it can be easily administered by lay persons.

Toxins TCD A & B of Clostridium Difficile for Horse Immunization

Dr. Sergey Artiushin,
University of Kentucky

Clostridium difficile is a bacteria that multiplies in the intestines of horses and other mammals when normal bacterial flora is poorly developed or becomes disrupted. Two very large and potent toxins are released by Clostridium difficile, causing massive damage to the intestinal lining. The resulting enterocolitis is an important component of the neonatal diarrhea complex. There currently is no vaccine, and treatment is expensive. This project seeks to generate antibodies in the horse to the parts of each toxin that bind to intestinal cells and thus block entry of the toxin. The work will involve cloning of polypeptides of toxins A and B, using recombinant DNA technology. Success should lead to a vaccine that could be administered to mares two months before foaling. The vaccine would provide colostral antibodies to the newborn foal.

Orthopedic and Genetic Roles in Wobbler Syndrome

Dr. James MacLeod,
University of Kentucky

Wobbler Syndrome carries a guarded to poor prognosis, and many afflicted horses are not good candidates for vertebral fusion and have to be euthanized. The focus of this project will be to examine the role of abnormal bone and cartilage formation in the neck vertebrae, and to identify regions of DNA and, potentially, even specific genes that are involved in Wobbler Syndrome. Technology will include three-dimensional X ray, Magnetic Resonance Imaging, and DNA isolation.



Track Banking and the Asymmetry of Hoof Loading

Dr. Jeffrey Thomason,
University of Guelph

This grant was selected by the board to receive the fourth annual Elastikon™ Equine Research Award. It is supported by a donation to GJRF from Johnson & Johnson's Consumer Products Division, manufacturer of Elastikon tape and other equine products.

With every stride at racing speed, forces acting on the legs reach as high as two to three times the horse's body weight. Avoiding any increased loading is intuitively regarded as beneficial in preventing injury. It is believed in theory that having no banking on the turns or too-low banking can increase the forces, but little scientific work on banking has been done since Swedish studies on Standardbred horses in the 1970s. This study aims to refocus attention on developing insight into the effects of different banking, by use of strain gauges. Additionally, the study will address the widespread practice of racing and training almost exclusively counter-clockwise in North America. Horses will be exercised in both directions and measurements will be recorded as to strains on different parts of the hoof in both directions.

Molecular Characterization of Neurovirulent Equine EVH-1 Strains

Dr. Udeni Balasuriya,
University of Kentucky

The increased incidence of the neurologic form of Equine Herpesvirus-1 has caused highly publicized problems at race tracks, farms, and other equine centers in

recent years. The Foundation has supported several projects on EHV-1, and this lab has discovered there are more types of mutations than were previously thought, which have impact on the prevalence of the neurologic strain of the disease. This project will attempt to identify further additional reputed neurovirulence determinants of EHV-1 by sequencing genes essential for replication. The researchers will utilize the University of Kentucky's extensive collection of EHV-1 isolates, collected over many years.

Pharmacokinetics/Pharmacodynamics of Quinapril in Horses

Dr. Jennifer Davids,
North Carolina State University

Antigen converting enzyme (ACE) inhibitors are frequently used in human medicine and small animal veterinary medicine to treat heart failure, chronic renal disease, and high blood pressure. One ACE inhibitor, Enalapril, has been studied in horses but found ineffective when given orally. This project will test whether another ACE inhibitor, Quinapril, is effectively absorbed by the horse's gastrointestinal tract. It has been shown to improve heart function of horses with valvular disease and atrial fibrillation, but is not yet widely used in horses because the absorption and pharmacological effects in the species have not yet been adequately studied.

Endotoxemia as a Predisposing Factor for Laminitis

Dr. Nicholas Frank,
University of Tennessee

Funded through NTRA Charities: There exists considerable circumstantial evidence that there is a relationship between endotoxin and onset of laminitis. This project seeks to verify that causal relationship and, if it successfully does so, would also

verify that use of anti-inflammatories has a valid scientific basis.

Equine Bone Regeneration with Adult Stem Cells

Dr. Mandi Lopez,
Louisiana State University

Adult stem cells in recent years have been the subjects of research to determine their potential to treat injuries in horses. Bone repair is one aspect which is being investigated. It requires about 70 million adult stem cells to repair a single cubic centimeter of bone. Only two types of tissues in mammals have been shown to have the potential to provide that many stem cells, i. e., adipose (fat) and bone marrow. The laboratory of this researcher has found that stem cells from both sources indicate the ability to form bone in cell experiments. Comparisons on the bone-forming abilities of fat-derived and bone-marrow-derived stem cells have not been done conclusively, and this project will address that important next question. The researchers

believe that “results from this study will significantly advance treatment of broken bones in the horse.”

CONTINUING PROJECTS FROM 2009

Antiviral Drugs To Combat Equine Herpes Virus-1 Infection

Dr. Arthur Frampton,
University of North Carolina-Wilmington

Prevention Of Equine Herpes Virus-1 Myeloencephalitis By Delayed Therapy

Dr. Lara Maxwell,
Oklahoma State University

Developing Equine Bone Morphogenetic Protein For Cartilage And Bone Repair

Dr. Matthew Stewart,
University of Illinois at Urbana Champagne

Effect of digital hypothermia on inflammatory injury in laminitis

Dr. James Belknap,
The Ohio State University

STORM CAT CAREER DEVELOPMENT AWARD

The Storm Cat Career Development Award was created to provide an early boost to an individual considering a career in equine research. The award is underwritten by board member, Mrs. Lucy Young Hamilton, and named in honor of the distinguished stallion Storm Cat, which was bred by Mrs. Hamilton’s father, W. T. Young, and stood at the family’s Overbrook Farm in Kentucky.

The fifth annual recipient is Catherine H. (Radcliffe) Hackett, a post-doctoral fellow from Cornell University. Her research entitled “Temporal Analysis of Megenchymal Progenitor Cells” receives the one year award of \$15,000. Dr. Hackett will be working with Dr. Lisa Fortier and Dr. Julia Flaminio.



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 March 2010.

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Notice: Upon request, a copy of the latest Annual Report filed by Grayson-Jockey Club Research Foundation, Inc. with the New York Secretary of State may be obtained from the Foundation (821 Corporate Drive, Lexington, KY 40503) or from the Secretary of State (162 Washington Ave., Albany, NY 12231).