# Equine Research News

A digital presentation of Grayson-Jockey Club Research Foundation

***Providers of Equine Research From 1940 thru 2016***

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## A Step Forward on EHV-1

*By Dr. Art Frampton Jr.*

Equine herpesvirus 1 (EHV-1) is the cause of significant illness in horses. Clinical signs that appear early after infection include fever, inappattence, malaise, coughing, and mucopurulent discharge.

While most horses recover from this infection with no long-lasting negative effects, some horses will experience serious complications resulting from EHV-1 infection including a neurological disease termed equine herpesvirus myeloencephalopathy (EHM). Clinical manifestations of EHM include fever, ataxia, incontinence, and partial to full paralysis.

> ***"Dr. Frampton's project showed for the first time how the EHV-1 virus is able to modulate the immune response of endothelial cells by gene regulation during infection ---one of the first steps in recognizing how the virus is able to seemingly hide from a horse's immune system."***
>
> ---Dr. Johnny Mac Smith
> *Grayson Veterinary Consultant*

Recently, there has been a significant increase in the number of neurologic cases caused by EHV-1 across the U.S. (USDA-APHIS, 2007) and previous studies have revealed a link between EHM and strains of EHV-1 that contain a specific mutation within the viral DNA polymerase gene ($A_{2254} > G_{2254}$). Data collected by various groups have shown that EHV-1 strains with this DNA Pol mutation are isolated at a higher frequency from horses afflicted with EHM compared to EHV-1 strains that do not contain this mutation

***In this edition:***



(Allen, 2007; Perkins et al., 2009; Pusterla and Hussey, 2014). Thus, EHV-1 strains that harbor the DNA pol mutation are now commonly classified as neurologic while those that do not harbor this mutation are classified as non-neurologic. While the DNA pol mutation is correlated with neurovirulence, it is not the sole factor that influences whether an infected horse will develop EHM. The currently available data support the hypothesis that EHM is multifactorial as 16-24% of EHM cases are caused by an EHV-1 strain that does not contain the DNA pol mutation (Perkins et al., 2009). Therefore, researchers and clinicians should be cautious when ascribing neurologic potential of EHV-1 based solely on the presence of the DNA Pol mutation.

Previous studies revealed that infection of endothelial cells within the central nervous system and the subsequent inflammatory response is another factor that contributes to the pathology observed in horses infected with EHV-1. In our Grayson-Jockey Research Club funded study (Johnstone et al., Veterinary Microbiology Vol. 192:52-59, 2016), we measured the expression levels of 49 host immune response genes after infection with 12 strains of EHV-1 with the aim to 1) identify key host inflammatory genes that are elicited after EHV-1 infection and 2) identify targets for therapeutic intervention of EHM. We identified a set of pro-inflammatory genes that are highly up-regulated after infection. The pro-inflammatory chemokines CXCL9, CXCL10, and CXCL11 were all up-regulated compared to mock-infected controls and, of all

of the host genes, CXCL11 was shown to be the most highly expressed after infection with each strain. Other up-regulated genes included CCL5, CCL8, IL6, CCL20, TNF, and TNFSF13B. Overall, results from these gene expression assays identified specific host immune genes that are modulated in endothelial cells after EHV-1 infection and revealed that known mediators of inflammation, including the CXCR3 ligands CXCL11, CXCL10, and CXCL9, are expressed to high levels. Due to the known role of these CXCR3 ligands in immunopathology, combined with their up-regulation in response to EHV-1, we hypothesize that these specific chemokines may play a major role in the pathology associated with EHM, most likely due to their ability to recruit lymphocytes to sites of infection. Future work will employ the CBA mouse model (Frampton et al., 2004) to directly investigate whether the CXCR3 ligands recruit T lymphocytes into the CNS of EHV-1 infected mice and also examine whether inhibiting these cytokines with non-steroidal anti-inflammatories (NSAIDS) including flunixin-meglumine, phenylbutazone and ketoprofen and specific signal pathway inhibitors can limit or block the CNS pathology observed in horses with EHM.

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## References

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## Foundation Supporters Named To Texas Horse Racing Hall of Fame

The Texas Thoroughbred Association recently announced that Hugh Fitzsimons and John T. L. Jones Jr. are in the class of 2016 to be inducted into the TTA Hall of Fame. Fitzsimons, Jones, and three others will be feted at the Hall of Fame Gala on October 29 at Retama Park. The rest of the class consists of Dr. Nat Kieffer, Jay Pumphrey, and the noted Quarter Horse First Down Dash.

The versatile horsemen Fitzsimons and Jones have been leaders in Texas and overall United States racing for many years. Jones has been a generous donor to Grayson while Fitzsimmons is a Rokeby Circle member of the Foundation, which he has been supporting since 2003. We thank both for their generosity and congratulate them on this honor.

TEXAS HORSE RACING HALL of FAME

## 2016 Research Call

Grayson-Jockey Club Research Foundation is now accepting grant proposals relevant to equine health and soundness. Deans and department heads at universities were contacted several weeks ago and asked to remind the equine researchers at their universities that the deadline for applications for research grants is Oct.3.
As usual, Grayson-Jockey Club Research Foundation is soliciting projects related to the range of illnesses, soundness, and management problems which can affect health and soundness of horses, regardless of breed or use.

The Principal Investigator of any project being developed for proposal is invited to the click here for the online application.

There are also two Career Development Awards offered this year through the Foundation. Only one application is necessary to apply for either the Storm Cat or the Elaine Klein Development Awards. The applicant must be working under the supervision of a tenured faculty member who is responsible for directing the post-graduate fellowship experience.
The long-term goal of this annual program is to spur development of potential career researchers by allowing post-graduate and post-residency students to further their experience with techniques and general research methods in areas under investigation by their institutions.
The deadline for the Development Awards application is Nov. 1, different from that for the regular. *Click here for more information and the Career Award application.*

### The Evaluation Process:

The process of evaluating grant proposals goal is designed to identify scientifically sound projects with the greatest potential impact on both the horse industry and the problem being studied.

The Research Advisory Committee (RAC) is composed of 32 equine research scientists and actively practicing veterinarians.
The concept is built on the premise that combining their skills during the evaluation process will result in the funding of the best possible research, aimed at the most important problems of the horse industry.

After the Oct. deadline, Dr. Johnny Mac Smith, the Foundation's veterinary consultant, distributes to the RAC basic information on all projects which have been submitted (usually between 50-70 annually). He requests that all RAC members alert him to any conflicts of interest. Conflicts might be as simple as the project coming from the university which also employs the RAC member. Other types of conflicts include whether the RAC member was a mentor to the Principal Investigator or other key personnel involved in the proposed research.

Once he is alerted to the conflicts, Dr. Smith assigns each project to a team of four members of the RAC who are charged with evaluating and filling out a score sheet for each project assigned. Assignments reflect the specific area of expertise of the committee members, matched with the subject and branch of science of the grants.

Each of the four reviewers judges a proposal using the criteria on the scoring sheet and writes a narrative review. One member of the team is designated as the Composite Reviewer and is sent the reports and scoring sheets from the others. The scores are tabulated and submitted to the Lexington office of the Foundation.

While there is a team of four carefully evaluating each grant, the entire 32-person advisory committee also studies each and every proposal.

The RAC annually meets in Fort Worth in late January for three days. The first step is for each four-member team to confer among themselves to resolve any wide disparity of their scores and re-calculate the composite score for the proposal if appropriate.

Secondly, under RAC chairman Dr. Steve Reed, the entire 32 person committee goes through each proposal one by one, with all members participating freely. (Anyone with a conflict leaves the room while the applicable project is being discussed.) The process takes an entire day. The next morning, the RAC reassembles and is shown the scores of each project resulting from the previous deliberations.

The projects which have scored well enough to qualify for potential funding are presented in descending order of the numerical score. Each project is then matched against the one below it, i. e, “Do you still prefer project 1 to project 2? Show of hands.” Marching through all the projects gives the opportunity to reconsider on the basis of importance of the project, proper budgeting, and, as always, the potential impact.

By the end of the process, the RAC has a list to recommend to the Grayson board of directors who will make the final decision at a board meeting. The board is provided synopses of the top projects and there is also a representative of the RAC to answer any questions. The final decision is based on the available budget for that year. In recent years, the Foundation has been in position to provide more than $1 million for equine research projects.

## Funding

A timeline is incorporated into the application document so that all investigators are aware of the schedule. The applicant in the original application predicts a specific schedule of progress. Almost all projects are scheduled for one or two years. The funding cycle commences April 1, with three equal payments being made through the year. A progress statement is expected on November 1 of the original funding year. However, there sometimes arise legitimate reasons for the principal investigator to request a no-cost extension from the Foundation, and these are granted on a per need basis. Satisfactory progress must be documented in order to continue receiving funding. Second-year funding must be approved by the Foundation Board following recommendation from the office.

The expectation for the end game of any project is that it be published in a peer reviewed scientific journal. Illustrating the efficiency of the process and the professionalism of the equine research community, the Foundation has had no projects default on this ultimate expectation.

# Saratoga Golf

## Tuesday • August 16, 2016

Saratoga National Golf Club • Saratoga Springs, NY

Registration and Lunch - 12:00 p.m.
Shotgun Start -1:00 p.m.
Cocktail Reception - 5:00 p.m.
Dinner & Awards Ceremony - 5:30- 7:30 p.m.

*Golf Outing Includes: Buffet lunch, golf, cart, green fees, on-course refreshments, open bar and dinner buffet*

Contests Include:
- Team Prizes
- Closest to the Pin
- Longest Drive

**Click here for tickets and sponsorship options**

## Grayson-Jockey Club Research Foundation, Inc.

*I wish to be enrolled as a member or donor of Grayson-Jockey Club Research Foundation as follows:*

| MEMBERSHIP LEVELS *(Check one)* | ANNUAL CONTRIBUTION |
|---|---|
| ____ ROKEBY CIRCLE | $10,000 or more |
| ____ Platinum Circle | $ 7,500 or more |
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