Use Of Nucleic Acid Vaccines To Protect From EHV-1/EHM

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This proposal is to develop a novel mRNA-based equine herpesvirus (EHV) vaccine that protects horses from EHV-1 myeloencephalopathy and will also likely cross-protect against other equine herpesviruses.

Equine herpesvirus-1 (EHV-1) infection results in sporadic but devastating outbreaks of neurological disease in the equine population caused by a myeloencephalopathy with a poorly understood pathogenesis. The impact of EHV-1 myeloencephalopathy (EHM) on equine health and the industry is highlighted by a series of major outbreaks in North America and Europe over the past decade, including the two largest outbreaks in 2011 and 2021 in North America and Valencia, Spain. Despite the importance of EHV-1 in horses, effective prevention remains elusive and there is currently no vaccine available to prevent EHM.

This is partially a consequence of the absence of a reliable experimental equine model of EHM and partially due to a lack of innovation in vaccine technology in the equine vaccine market in the past 40 years. In this proposal, five investigators with complementary expertise in equine herpesvirus virology, vaccinology and pathogenesis/animal models have come together to close a major gap in vaccine development against EHV infection. The goal of this application is to exploit innovations in RNA vaccine technology that have come about during the COVID-19 pandemic and are currently the first line of defense.

We propose to refine this mRNA vaccine technology for immunization of horses. Based on our extensive preliminary data, we will test vaccines containing the parts of EHV-1 that are important for inducing protective immunity in horses. We are ideally placed to accomplish this task because we have previously developed a unique model for experimentally inducing EHM in horses that now allows us to test potential vaccine candidates . Moreover, given the high degree of similarity among equine herpesviruses genetically related to EHV-1, namely EHV-3, EHV-4, EHV-8 and EHV-9, our vaccine candidates, if proven successful, are likely to also offer protection to other equine herpesviruses. Additionally, they could readily be extended as a platform to induce protective immunity against an array of EHVs or other equine viruses.

Importance to the Equine Industry: The EHV-1 “G” strain (SNP at ORF 30, G2254) has been associated with more severe outbreaks and a greater occurrence of EHM than the EHV-1 “A” strain (A2254 genotype). The enhanced replication capacity with the “G” strain appears to be associated with an enhanced frequency of more severe disease; however, both strains cause EHM. Several factors appear to be contributing to an uptick in EHV-1, particularly in Europe and the United States, with equine venues being closed or quarantined as a consequence. We propose an mRNA vaccine delivered in an extended release, biodegradable polyanhydride vaccine depot. Compared with traditional vaccines, we anticipate that this approach will be more effective and require fewer inoculations.

Funded by

FM Area Foundation
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Funded by Grayson-Jockey Club Research Foundation