Use Of Equine IFNL3 mRNA For Prevention Of EHV-1 And EHM

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This study proposes to develop IFNL3(gene that encodes anti-viral defense) mRNA administration in horses as a treatment for EHV-1 and EHV-1 myeloencephalopathy and as booster for EHV-1 vaccination.

Equine Herpesvirus-1 (EHV-1) is a common virus in horses that can cause serious problems including respiratory illness, abortion in pregnant mares, newborn foal death, and a severe neurological condition called EHM (Equine Herpesvirus Myeloencephalopathy). EHM is the most devastating form of the disease, and 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 and EHM, there are currently no vaccines available that can prevent or control EHM. In addition, the research on therapeutics is lacking. This is why in this proposal, our team with complementary expertise in areas of equine herpesviruses, vaccine development, immunology, and RNA technology and delivery, have come together to find new solutions to protect horses from this virus and the devastating consequence of EHM.

The focus of our proposal is on using a special immune protein called interferon lambda 3 (IFNL3), which helps the body fight off viruses. It works similarly to other interferons but with fewer side effects and less inflammation.
In previous studies, IFNL3 has been shown to protect against neurological disease caused by other herpesviruses by reducing the virus's ability to multiply and thrive in the body, and helping the body build strong immunity, all of which are important in preventing EHV-1 and EHM.
Our group has already shown that IFNL3 can reduce the amount of EHV-1 in cell culture. However, making enough of this protein for use in horses is difficult. To solve this problem, we want to use mRNA technology, which teaches the horse's body to make the IFNL3 protein itself, similar to how COVID-19 mRNA vaccines work in humans.

The main idea of our proposal is that IFNL3 mRNA could be used both as a treatment option to prevent EHV-1 infection and as an added boost (called an adjuvant) to make existing vaccines work better. To test this, we plan to:

1. Study how IFNL3 affects the virus in horse airway cells and whether it can stop the virus from reaching the spinal cord.
2. Find the right dose to safely trigger a strong immune response in actual horses.
3. Test whether combining IFNL3 mRNA with a vaccine improves the horse's immune protection.

In summary, this project's goal is to identify new and better ways to prevent and treat equine herpesvirus infections, including EHM. It could also introduce IFNL3 mRNA as a promising new tool for treating other equine viruses or improve vaccines, not just for EHV-1, but also for other horse viral diseases whose protection depend on similar immune responses.

Importance to Industry: Equine herpesvirus 1 (EHV-1) neurological disease (EHM) continues to cause significant disease and extensive economic losses through closure of race tracts and sales barns, delays in training schedules and death of valuable animals. The substantial impact of EHV-1 on equine health is highlighted by a series of major outbreaks in North America and Europe over the past decade resulting in fatalities and enormous financial costs to the equine industry. Major outbreaks of EHM remain a problem demonstrating the fact that current vaccination strategies have not shown to offer protection from EHM.

We propose address this problem, by using novel RNA technologies to deliver a natural protein called interferon lambda 3 (IFNL3) to the horse based on the success of the current COVID-19 vaccines that employ this technology.

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Using RNA technology, we will get the horse's immune system to produce and boost the naturally produced IFNL3 itself to fight of EHV-1 (and other viruses) more effectively.

This strategy was chosen based on the knowledge that horses that don't get EHM after exposure to EHV-1 tend to have a strong and timely interferon response, which is a key part of the immune systems way to fight viruses. IFNL3 plays a major role in triggering that response. In addition, we have shown that IFNL3 can slow down or stop EHV-1 from multiplying, which is a very promising sign.

By the end of this project, we hope to offer a new treatment or preventive tool for protection from EHV-1, not just as a standalone therapy, but also as a booster for vaccines. This approach might also help protect horses against other viral diseases that rely on interferon responses to control infection.

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