improving a VapA mRNA Vaccine For R. Equi In Foals

Noah Cohen, Texas A&M University –Two Year Grant

The aim of this study is to improve the design of a mRNA vaccine for foals to provide stronger, longer immunity against Rhodococcus equi, a leading cause of disease and death in foals worldwide.

Great need exists to develop an effective vaccine against Rhodococcus equi (R. equi) pneumonia of foals because of the importance of this disease to the equine industry. Our long-term goal is to develop a messenger RNA (mRNA) vaccine to protect foals against pneumonia caused by R. equi. The vaccine target will be the virulence associated protein A (VapA) of R. equi. The rationale for targeting VapA is that it is necessary to cause disease in foals, it induces robust immune responses in foals after vaccination or natural infection, and antibody activity against VapA in foals is associated with lower odds of rhodococcal pneumonia (i.e, higher anti-VapA antibody levels are associated with protection against pneumonia). A prototype VapA mRNA vaccine that we developed initially appeared to induce good immune responses in foals, but in a study conducted during 2024 the same vaccine was not highly effective at stimulating immune responses in foals, leaving some foals unprotected against experimental infection of their lungs with R. equi.

In this project, we aim to improve upon our prototype vaccine by designing the mRNA to include a protein known as lycosylphosphatidylinositol (GPI) that will attach VapA protein to the surface of cells at the site of injection. This anchoring will allow for greater exposure of the immune system of vaccinated foals to the VapA protein. In other species of mammals, anchoring with GPI has been demonstrated to result in longer lasting and stronger immune responses to anchored vaccine targets. In our first aim, we propose to demonstrate that the anchored VapA mRNA vaccine – but not our prototype (original) VapA mRNA vaccine - is expressed on the surface of equine cells grown in the laboratory into which the mRNA has been introduced.

In our second aim, we will compare the antibody levels against VapA of foals immunized intramuscularly (IM) at ages 1 and 21 days with our new anchored VapA mRNA vaccine to those of foals immunized IM at the same ages with our prototype (original) mRNA vaccine. We expect to find that a construct of mRNA can anchor VapA to equine cells and that young foals vaccinated with this anchored mRNA will develop more robust and longer-lasting immune responses. If we are successful, this anchored mRNA vaccine could be advanced to assessing its ability to protect foals against infection with R. equi.

Importance to the Equine Industry: The horse industry remains an agriculturally and economically important venture in the U.S., generating over $177 billion in total production in 2023 according to the American Horse Council. Producing healthy foals is necessary to maintain and improve the nation's horse population, and the health of foals is important to the horse industry from a welfare perspective. Infectious diseases are leading causes of disease and death in foals, and pneumonia is a principal infectious disease of foals. Respiratory disease was the most common cause of disease and death in foals in Texas, and ranked 3rd as a cause of morbidity and 2nd as a cause of mortality in U.S. foals 1 to 6 months of age. R. equi is considered the most common cause of severe pneumonia.

The disease is endemic at many horse-breeding farms with cumulative incidence often around 20% to 40% of the foal population. Although rigorous, systematic economic impact studies for this disease are lacking, it is widely recognized that the costs resulting from veterinary care, long-term therapy, and mortality of some foals are very high at affected farms. In addition to significant immediate costs, R. equi pneumonia can have a long-term detrimental effect on the equine industry because it has been reported that North American foals that recover from the disease are less likely to race as adults and performance was diminished by this disease for some Australian Thoroughbreds.

Funded by Grayson-Jockey Club Research Foundation