



## GRAYSON RESEARCH USING mRNA THROUGH INHALATION THERAPY TO TREAT FOALS FOR *RHODOCOCCLUS equi*

Included in the 2021 Grayson-funded projects is a groundbreaking project that is using a vaccine composed of lab-made messenger RNA molecule (mRNA), which provides passive immunization of foals against *Rhodococcus equi*. This research is a joint study with Dr. Jeroen Pollett of Baylor College of Medicine and Dr. Noah Cohen of Texas A&M University. We recently interviewed these two established researchers about this exciting project.



**Dr. Jeroen Pollett**  
Baylor College of Medicine



**Dr. Noah Cohen**  
Texas A & M University

### What is the current treatment for *R. equi*?

**Dr. Noah Cohen:** The current treatment of choice is a macrolide antimicrobial, with some debate about whether or not to combine rifampin with the macrolide. Ancillary treatments include anti-inflammatory drugs, bronchodilators, additional antimicrobial agents, and probiotics or other anti-diarrheal products to help with diarrhea caused either by the antimicrobial drugs or the *R. equi* infection itself (although *R. equi* primarily infects the lungs, it can also infect other sites including the intestinal tract). The course of treatment often lasts for weeks and can thus be expensive. The macrolide antibiotics have associated risks, including diarrhea in the foals and occasionally their dams, and hyperthermia (overheating/failure to dissipate heat). Since *R. equi* can also infect sites other than the lungs (such as the eyes, intra-abdominal lymph nodes, intestinal tract, bone, etc.), specific additional treatments may be required for these extra-pulmonary infections.

### Why is aerosolization of mRNA into the foal's lungs more effective than vaccinating the foal?

**Dr. Noah Cohen:** Delivering mRNA to the lungs is important because the *Rhodococcus* are inhaled, and the lungs are

the primary site of infection. It is our belief and hope that directly producing antibodies in the lungs will more effectively prevent pneumonia caused by *R. equi* than does transfusing plasma from donors that are hyperimmunized against *R. equi*.

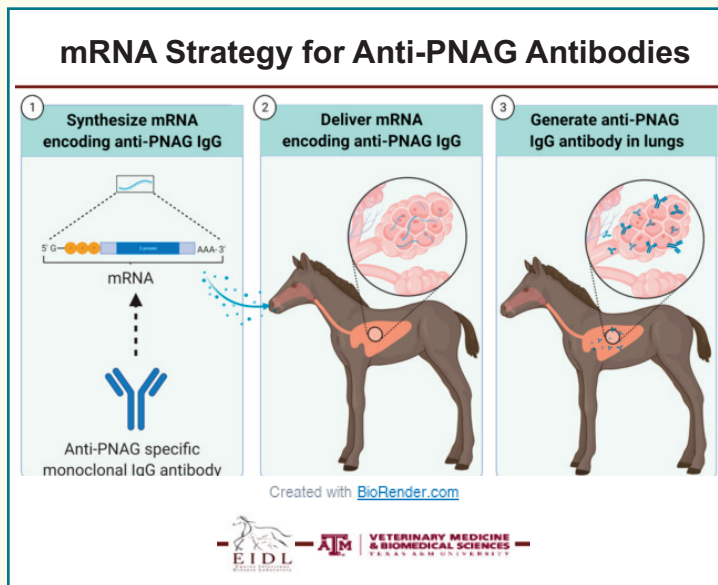
In reference to this project, it is important to clarify the distinction between active and passive immunization. Active immunization is the process of being given a vaccine. For example, the Moderna and Pfizer vaccines against COVID-19 have mRNA that gets translated into a protein of the virus that causes COVID-19 (known as SARS-CoV-2), and our bodies then recognize that protein and make antibodies against it to protect us against SARS-CoV-2.

**Dr. Jeroen Pollett:** Active immunization has both advantages and disadvantages. Advantages: A vaccinated individual is generally protected for a very long time (one to 30 years).

Disadvantages: It takes at least four weeks before immunity is reached after vaccination. In that time period the individual is still susceptible to infection. In addition, the immune system of newborns is often not immediately

capable to generate a strong immune response by itself. In the context of *R. equi*, this means it will be difficult to protect vulnerable newborns in their first months of life.

*Dr. Noah Cohen:* Passive immunization is when antibodies are directly transferred to a host to protect it against infection. In the context of COVID-19, examples include convalescent serum, antibodies made in horses against proteins of the SARS-CoV-2, or monoclonal antibodies like the ones that were given to President Trump. In the context of *R. equi*, the only licensed product proven to reduce the incidence of *R. equi* pneumonia at farms is the transfusion of hyperimmune plasma. What we are doing in this project is providing mRNA that encodes for antibodies that will target *R. equi*, so our mRNA is designed for passive immunization.



*Dr. Jeroen Pollet:* Passive immunization also has both advantages and disadvantages. Advantages: A passively vaccinated individual is immediately protected after treatment. Hence, our foals potentially will be protected against *R. equi* from day one after we aerosolize the mRNA in the lungs. Disadvantages: Passive vaccination typically only offers protection for two to three weeks, after which it

requires a booster or the antibody level will again drop below the protection levels. A vaccine may also be given in parallel to induce both short- and long-term protection.

**Is this process of immunization by aerosolization expensive? In other words, if this treatment were to be available to the public at some point, would it be affordable for the majority of horse breeders?**

*Dr. Noah Cohen:* As others can attest, passive immunization with hyperimmune plasma is not cheap! These are early days of mRNA therapeutics and vaccines, but I expect the costs for mRNA to fall just as costs for real-time PCR (polymerase chain reaction), gene sequencing, and other technological innovations have fallen. Ultimately, this will be less expensive, safer, and – we hope – at least as effective (we believe more effective) than plasma transfusion. It is an innovative approach that hasn't yet been tried in anything other than a mouse, so we're excited to be on the leading edge of this field.

**Were there any adverse effects of the aerosolization procedure in any of the foals that were immunized?**

*Dr. Noah Cohen:* Thus far, we've observed no adverse effects.

**What other use in horses do you envision for the mRNA transfusion technology?**

*Dr. Noah Cohen:* We expect to be able to deliver antibodies for other bacterial and viral respiratory tract infections and for making vaccines, including vaccines against *R. equi*.

**How long have you been working with mRNA technology?**

*Dr. Noah Cohen:* My work with mRNA started with this project which resulted from my hearing Dr. Pollet speak at an international conference and reaching out to ask him about collaborating. Dr. Pollet has more extensive experience with mRNA for passive and active immunization because he was an early adaptor of this technology. My laboratory is very fortunate that Dr. Pollet was willing to consider working with horses.

## VET CHATS

Visit the video section of our website to review the webinar of *Dr. Cohen and Dr. Pollet* with an in-depth discussion on their project: **TREATING RHODOCOCCLUS EQUI BY INHALATION THERAPY**

**OTHER VET CHATS ARE ALSO AVAILABLE**





## One Foal's Journey With *R equi*

*Resia Ayres has been the operations manager of Grayson since 2008. She and her husband, Ken, are active Thoroughbred owners and breeders, usually breeding a single mare each year and racing the foal. This is the story of their 2021 foal.*

We were very pleased with our late February foal, a spunky colt by Dominus that was well-developed and sharp. This was our fourth foal out of the mare and appeared to be one of the best, so we were surprised in mid-May when we received a phone call from Laura Cain at Delaverne Farm with the news that our colt was experiencing difficulty breathing.

She asked the farm vet to come out and scan his lungs. The scan revealed a serious case of *Rhodococcus equi*, requiring hospitalization. Although we were aware of the malady, in all the years of breeding 30-plus foals, we had never experienced this infection.

The pair was vanned to the McGee Medicine Center at Hagyard Equine Medical Institute under the care of

Dr. Rana Bozorgmanesh (Dr. B), who wrote the following assessment:

*“Upon arrival, the 3-month-old colt had good body condition but was breathing hard with flared nostrils and a worried look in his eye. He had been seemingly normal the previous day and was suddenly found struggling to breathe and about to embark on the fight of his life. Unfortunately, this is not an uncommon presentation of *Rhodococcus equi* pneumonia in foals presented to our hospital. *Rhodococcus equi* is ubiquitous in the environment of horse farms and is present in the manure of most mares. Infection is thought to occur due to inhalation of airborne bacteria during the first couple of days of life, although the disease progresses slowly and insidiously, with a lot of foals showing no clinical signs until they have developed abscesses in their lungs. Clinical signs include fevers, lethargy, coughing, nasal discharge, and, in cases like this foal, difficulty breathing.*

*“His condition was complex, not just involving the primary infection, but he was also demonstrating significant associated inflammation. His difficulty breathing had developed as a complication of the infection, triggering an overwhelming and uncontrolled inflammatory reaction in his lungs, and it was the inflammation that could kill him. This inflammatory reaction can occur with any infection, although we see it most commonly*

*with *Rhodococcus equi* in foals admitted to our hospital. Treatment of these dynamic cases is multifaceted and involves antimicrobial therapy to address the underlying infection, as well as aggressive therapy to suppress the inflammatory response and improve oxygenation. Such therapy includes intranasal oxygen insufflation, bronchodilators and judicious use of corticosteroids. Prognosis for these foals is guarded, and they can deteriorate rapidly despite our best efforts.”*

Dr. B explained that treatment would be intensive and expensive with no guarantee that he would recover. As we watched our colt struggling to breathe, the prognosis did not seem good. When the doctor said it took three technicians to restrain him for intranasal oxygen cannula placement, it gave us hope that he would fight this infection with that same determination.

After reviewing our finances, she outlined a plan to give him the best chance at survival and still mitigate expenses. We would keep him hospitalized on oxygen for a few days and then remove the tube at night to see how well he could breathe on his own the next morning. The next day, we were excited to learn that while he was still critically ill, he could be released to a farm that could provide 24-hour care.

Our mare and foal were taken to Phoenix Farm to begin the long treatment process. This included an intensive list of various pharmaceuticals being administered through a nebulizer, a catheter, and orally on a 24-hour schedule. The pair was stall-bound for several weeks. Keeping the foal cool was essential to help the foal breathe, so a very large fan was placed at the entrance of the stall. Kathie Maybee, the owner/manager of the farm, was very hands-on with the colt. She had her work cut out, not only because of the rigorous dosing schedule, but because this guy, despite his illness, had attitude and size for a 3-month-old foal. Dr. B consulted with the farm vet, Dr. Michael Hughes, on the colt's condition, scans and blood-work, coordinating the next phase of his treatments.

This journey began on May 13<sup>th</sup> and now at the end of June, we are seeing the light at the end of the tunnel. Blood-work indicates the foal may discontinue the drug therapy. He will be scanned again and rechecked but his next task is to get back to doing what he loves—running around the paddock and showing off. We are indebted to the researchers, veterinarians, farm managers, grooms, and everyone else who had a hand in saving his life.



*Foal in April, prior to falling critically ill.*



*Dr. Rana Bozorgmanesh*



*Catheter used to administer drugs.*



# 2021 Educational and Sponsorship



## Palomino World Show

July 6-17 • Illinois State Fairgrounds • Springfield, IL



## Lexington Junior League Charity Horse Show

July 12-17 • Kentucky Horse Park • Lexington, KY



## United States Pony Club Festival

July 19-26 • Kentucky Horse Park • Lexington, KY



## Rood and Riddle Hats Off Day

July 31 • Rolex Arena, Kentucky Horse Park • Lexington, KY



## U.S Dressage Festival of Champions

August 24-29 • Lamplight Equestrian Center • Wayne, IL



## USEF Pony Finals

August 9-15 • Kentucky Horse Park • Lexington, KY



## USEA American Eventing Championships

August 30 - September 5 • Kentucky Horse Park • Lexington, KY



## All American Quarter Horse Congress

September 28 - October 24 • Ohio Expo Center • Columbus, OH



## T.I.P Championship Horse Show

October 8-10 • Stable View • Aiken, SC



## Retired Racehorse Project

October 11-17 • Kentucky Horse Park • Lexington, KY



## National Horse Show

October 27 - November 7 • Alltech Arena, Kentucky Horse Park • Lexington, KY



## AQHA World Show

November 1-20 • OKC Fairgrounds • Oklahoma City, OK



## USDF Dressage Finals

November 11-14 • Kentucky Horse Park • Lexington, KY



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