RESEARCH PROGRESS REPORT SUMMARY

Grant 02829: Investigating the Potential of Phage Therapy to Tackle *Staphylococcus pseudintermedius* Infections in Dogs

Principal Investigator: Gavin Paterson, PhD

Research Institution: R(D)SVS and Roslin Institute, University of Edinburgh

Grant Amount: $99,830

Start Date: 1/1/2021 **End Date:** 4/30/2022

Progress Report:

Report Due: 4/30/2022 **Report Received:** 4/29/2022

(The content of this report is not confidential and may be used in communications with your organization.)

Original Project Description:

The spread of antimicrobial resistance is a major threat to modern medicine, for both humans and animals. In the case of dogs, *Staphylococcus pseudintermedius* is an important cause of infections, especially pyoderma. Antimicrobial resistance in *S. pseudintermedius* is making infections more difficult to treat which is affecting dog welfare and might pose a threat to humans too. There is a need to explore alternative treatments to antibiotics with one approach being to use phage therapy. This therapy uses naturally-occurring viruses, called bacteriophages (phages) which infect and kill bacteria to treat bacterial infections. Phage therapy has a long history of safe and effective use in humans and has the advantage that it can target drug resistance bacteria with few side effects. This project has a team of veterinarians and scientists working together to isolate and characterize phages that kill *S. pseudintermedius* which may contribute to the development of new, exciting treatments to benefit dog health and wellbeing.

Publications: None at this time.

Presentations: None at this time.

Report to Grant Sponsor from Investigator:

Antibiotics are widely used in companion animal medicine and bring significant benefits to pet health and well-being. However, the spread of antibiotic resistance (AMR), where bacterial infections can no longer be treated successfully, is challenging their successful use in veterinary medicine. This is also a

One-Heath problem, as AMR readily spreads between animals and humans. The continued spread of AMR would have a devastating impact on animal welfare. Morbidity and mortality to infections would increase hugely; even routine infections that are currently treatable could become life-threatening. The increased difficulty in treating infections could render much of modern veterinary medicine (such as critical care, complex operations, and cancer treatment) almost impossible. There could be further indirect impacts of AMR to pet welfare - if treatments become more expensive owners might decline them or be deterred from seeking treatment in the first place leading to increased animal suffering, abandonment, and euthanasia.

It is therefore critical for pet animal welfare to tackle the problem of AMR. One attractive strategy is to identify new alternative therapies that could be used instead of, or alongside, antibiotics. In this project, we investigated the potential to use bacteriophages, viruses that kill bacteria, to treat canine bacterial infections. There are several exciting examples of the successful use of phage therapy in human medicine to treat multidrug-resistant bacterial infections. However, despite the promise of phage therapy, little work has been done to exploit this approach in veterinary medicine. Our work targeted the bacterium Staphylococcus pseudintermedius, which is a common cause of chronic AMR-infections in pet dogs (particularly skin infections).

Despite an extensive screen with over three thousand two hundred tests, we did not find phages that can readily kill this bacterium. While disappointing, this finding might hint at important information about the bacterium and how it interacts with phages which could still be useful in combatting it in the future. We also evaluated a series of phage proteins predicted to break open and kill bacterial cells. In our initial experiments, we failed to see any antibacterial effect. However, the resources generated in this project and now available to continue the work and it may be possible in the future to optimize the production and purity of these products and detect antibacterial activity.

In short, our project has highlighted the difficulty in developing much-needed new treatments against *Staphylococcus pseudintermedius.* Nonetheless, the work has generated new data and tools that improve our understanding of this bug and which may help the development of new treatments in the future. Tacking this challenge would not be possible without the kind support provided by the AKC CHF and we look forward to updating you further in due course on further outputs from our work.