Scientists identify novel approach for bacteriophage treatment of Clostridium difficile infection

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The team at Leicester has been working with common white waxworms available in the UK. Credit: University of Leicester

University of Leicester scientists have previously identified the potential

of using a bacteriophage cocktail to eradicate *Clostridium difficile* infection (CDI) and in this research, using an insect model, they show that their prophylactic use can prevent infection forming in the first place.

The data, which is the result of research conducted by University of Leicester researchers Janet Nale, Ph.D. and Professor Martha Clokie, both from the Department of Infection, Immunity and Inflammation, demonstrated that *C. difficile* phages are particularly effective when used to prevent infection, but they are also good at targeting harmful bacterial infections once biofilms have formed.

Using biofilm and waxworms as models, these phages reduced *C. difficile* bacterial counts when administered as a preventative measure. Furthermore, combinations of phages and vancomycin led to a marked decrease in *C. difficile* colonisation in the waxworms.

The fact that this was an experimental lab study in waxworms means that conclusions can be made about cause and effect in this species.

Phages have not been used in humans to treat CDI and to see whether these results apply to people, an experimental trial with people would be necessary. However, work with insect models is crucial to our understanding of how best to exploit them. They have shown that these new models are useful tools in which to investigate the timings and dose regimens of phage treatment.

The paper is now published online and is expected to be published in a hard copy special issue of Frontiers in Microbiology dedicated to the past, present and future of phage research and development.

The study was funded by AmpliPhi Biosciences Corporation, a global leader in the development of bacteriophage-based antibacterial therapies

to treat drug-resistant infections.

Professor Martha Clokie has been investigating an alternative approach to antibiotics, which utilises naturally occurring viruses called bacteriophages, meaning 'eaters of bacteria', for nearly a decade at Leicester.

She said: "The results suggest that it may be possible to reduce the threat of *C. difficile*, and potentially other bacterial infections, through the use of phages both prophylactically to prevent infection, and as therapy once an infection is established. Phage therapy targets specific pathogenic bacterial populations while sparing patients' beneficial microbiome."

M. Scott Salka, CEO of AmpliPhi Biosciences, said: "The data support our products' great potential in addressing antibiotic resistant and difficult to treat infections, including *C. difficile*. I would like to commend Dr Nale and Professor Clokie for their exciting and insightful research demonstrating the immense promise of phage therapeutics. Their findings underscore our enthusiasm for the potential of our proprietary platform to enable the development of therapeutics to treat a broad range of bacterial infections that are resistant or have suboptimal responses to current antibiotic therapies."

More information: Janet Y. Nale et al. 'Get in Early'; Biofilm and Wax Moth (Galleria mellonella) Models Reveal New Insights into the Therapeutic Potential of Clostridium difficile Bacteriophages, *Frontiers in Microbiology* (2016). DOI: 10.3389/fmicb.2016.01383

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