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Bacteriophage cocktail shows significant promise for Clostridium difficile infections

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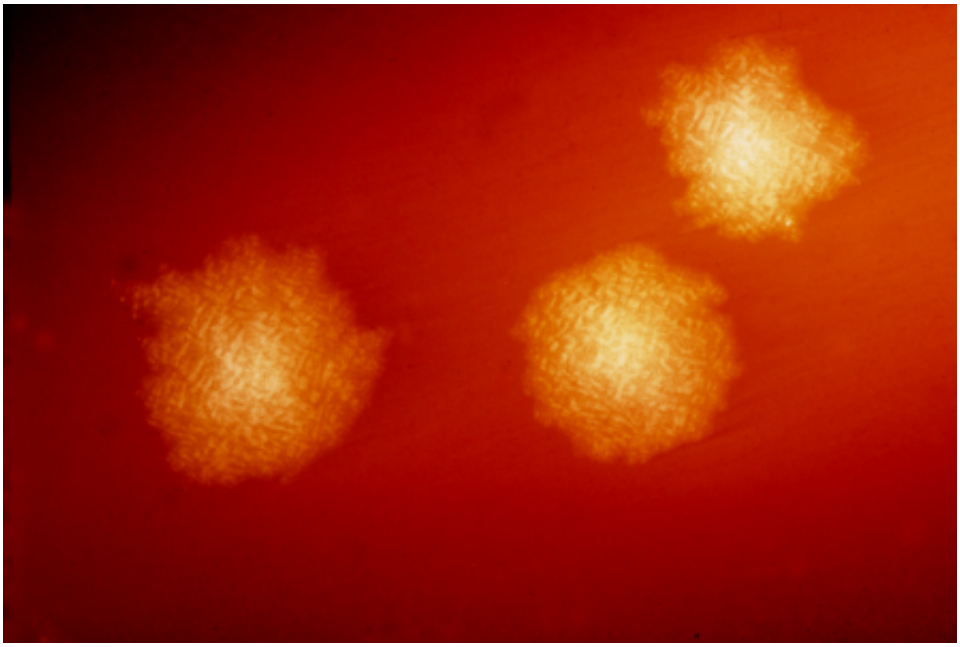

This photograph depicts Clostridium difficile colonies after 48hrs growth on a blood agar plate; Magnified 4.8X. C. difficile, an anaerobic gram-positive rod, is the most frequently identified cause of antibiotic-associated diarrhea (AAD). It accounts for approximately 15–25% of all episodes of AAD. Credit: CDC

A new University of Leicester study has confirmed the therapeutic potential of bacteriophage combinations to treat highly infectious bacteria C. difficile infections (CDI) while retaining a healthy gut.

A team led by Martha Clokie, Professor of Microbiology at the

University of Leicester's Department of Infection, Immunity and Inflammation, demonstrated that bacteriophage combinations significantly reduce growth of C. difficile cells and proliferation in complex models, whilst retaining healthy gut by preventing destruction of beneficial bacteria caused by traditional antibiotic treatment.

The study, which was funded by AmpliPhi Biosciences, is published in the peer-reviewed publication *Antimicrobial Agents and Chemotherapy*.

CDI is responsible for approximately 39% of the cases of antibiotic-associated diarrhoea in the Western world. Ten percent of CDI patients die due to lack of effective therapies. The main obstacles to preventing CDI are the existence of diverse C. difficile strains that vary in their response to antibiotics and the impervious nature of the C. difficile spores.

Results from studies carried out by Dr Janet Nale in Professor Clokie's laboratory demonstrated that specific phage combinations caused the complete destruction of C. difficile and prevented the appearance of resistant bacteria, while results of the complex models work showed that oral delivery of optimised phage combinations resulted in reduced C. difficile spread at 36 hours post-infection.

Additionally, the phage combination was able to kill 12 of the 13 C. difficile variants that are most prevalent in the UK, and were effective against the emerging variants that are increasingly causing concern in the UK, the US and more widely. The phage combination also reduced or completely prevented regrowth of C. difficile when compared to treatment with individual phages.

"Our data supports the therapeutic potential of phage combinations to treat C. difficile infections," said Professor Clokie. "In particular, combinations of phages optimised in the laboratory setting were shown

to be effective in the treatment of C. difficile in animals. Further refinements to our bacteriophage cocktails can be explored to maximise phage efficacy and to target the most dominant C. difficile variants."

"Lab experiments, like this, allow us to see what effect specific phage combinations have on C. difficile in complex models. To see the effect of specific phage combinations in humans we would run an experimental trial with people."

M. Scott Salka, CEO of AmpliPhi Biosciences, added: "The prevalence of C. difficile, the high costs of infection control and the challenge of finding alternative treatments, all contribute to the significant clinical and financial burden that CDI imposes on healthcare systems. The positive outcomes of these studies validate phage-based therapy as a promising approach that has the potential to address the growing challenge of CDI. We look forward to our continued collaboration with Professor Clokie to develop tailored and customised phage therapies for future clinical trials in humans."

More information: Janet Y. Nale et al. Bacteriophage Combinations Significantly Reduce Clostridium difficile Growthand Proliferation, *Antimicrobial Agents and Chemotherapy* (2016). DOI: 10.1128/AAC.01774-15

Provided by University of Leicester