Cytophage Technologies Inc.
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CYTOPHAGE

Harnessing the power of bacteriophages against antimicrobial resistance

Cytophage has developed a versatile bacteriophage-based antibacterial and antiviral technology targeting human and agricultural infectious diseases. With lead programs in avian and swine bacterial infections and in COVID-19, the company is seeking to expand its partnership network.

Cytophage, a bacteriophage (phage) biotech company based in Winnipeg, Canada, uses a synthetic biology approach to develop phage therapies that can help address bacterial challenges in human health and agriculture. The company's approach consists of engineering phages that specifically target infectious bacteria of interest and contain combinations of genetic factors designed for maximum antibacterial effect in humans, animals and agricultural crops, as well as on surfaces in health care or food processing facilities. The company's lead animal health products include phage cocktails to treat *Salmonella enterica*, serovar Enteritidis; avian pathogenic *Escherichia coli*; and *Clostridium perfringens* in poultry. Discovery programs in swine *Streptococcus suis* infections and cow mastitis are also on the go. Further, Cytophage is currently evaluating opportunities to enter the human health market, including compassionate use phage therapy, a phage-based COVID-19 vaccine and a second phage-based human vaccine for respiratory viral infections.

"At Cytophage we have harnessed bacteriophages, nature's elegant and sophisticated approach to eliminating bacterial infection and contamination, to target a number of important agricultural pathogens. We have shown that they also provide a powerful platform for developing human vaccines," said Steven Theriault, CEO and CSO of Cytophage. "Our vision is to work with our development partners to bring products to market that will allow every hospital, every veterinarian and every agricultural facility to have alternative products to existing anti-infectives for effectively managing a broad range of known and emergent pathogens."

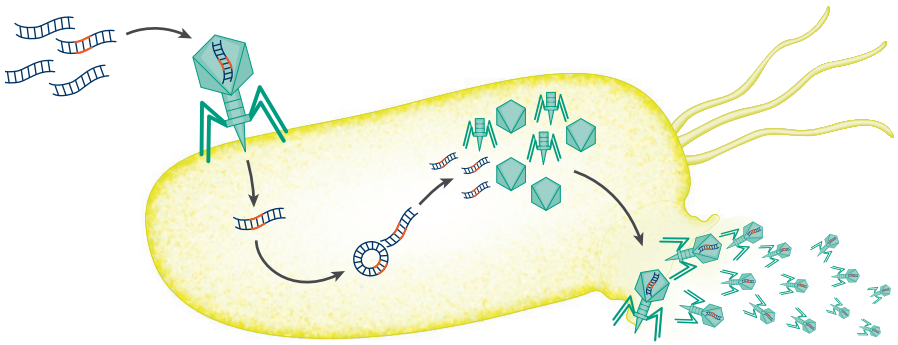

Fig. 1 | Engineering bacteriophage-based antibacterial agents. Cytophage has developed a versatile technology for the rapid engineering of traits, such as lytic, structural, attachment and other functions, into bacteriophages. The resulting bacteriophage agents attach to the targeted bacteria of interest (yellow structure), insert their genetic information, replicate using the host bacterium's machinery before destroying it, and move on to kill more bacteria.

Phages—solving the world's antimicrobial conundrum

Historically, antibiotics ushered in a new era in medicine by helping to reduce deaths from pervasive infectious diseases, such as cholera, typhus and scarlet fever. However, rampant overuse of this indispensable medical tool—globally, an estimated 100,000–200,000 tons of antibiotics are now used annually between health-care and agricultural applications—has led to an alarming rise in antimicrobial resistance[1] (AMR). Approximately 70% of all antibiotics are used in the animal industry, resulting in the generation of superbugs, microbes resistant to one or more antibiotics, that can in turn infect human populations. Indeed, the World Health Organization (WHO) predicts that worldwide and by 2050, 10 million people will succumb to antibiotic-resistant superbugs every year. Beyond efforts to slow down the rise and spread of AMR and a concerted effort to develop novel antibiotics that target alternative mechanisms to those targeted by existing antibiotics, other strategies are needed to diversify the antimicrobial toolbox.

Phages have recently emerged as a potentially powerful way to target infectious bacteria with few side effects and much lower risk of developing resistance[1]. Phages are bacteria-specific viruses that play a critical role in regulating bacterial populations in nature. Their therapeutic potential has long been known, but only recently has it begun to be translated into actual applications owing to the development of synthetic biology tools for modifying phages.

Cytophage has developed a versatile technology that allows for the rapid engineering of phage traits, such as lytic, structural, attachment and other functions, through targeted manipulation of its genes (Fig. 1). Importantly, the engineered phages are grown on a yeast background rather than the original target bacteria, providing scalable, rapid and contamination-free virus manufacturing capacity. For animal applications, phages can be mixed with animal feed for high-dose treatments, added to the water system for low-dose treatments, or used as a spray to disinfect barns and cages or other surfaces of interest.

Arming phages to combat viral infections

The versatility of Cytophage's technology has come to the fore in the COVID-19 pandemic. The company was able to rapidly produce a potential COVID-19 vaccine by recasting phages as a platform on which to display epitopes of interest obtained from screening convalescent plasma and identifying the most prevalent epitopes. A cocktail of phages decorated with four different COVID-19 epitopes is currently in advanced preclinical studies for intranasal administration. This novel use of phages against viral infections, not just bacterial infections, has huge implications for the company and for the use of phages as therapies. Cytophage is now exploring additional antiviral programs that could benefit from using phages as a vehicle for triggering a safe and potent virus-specific immune response in humans.

"Capturing the potential of bacteriophages in addressing the looming antibiotic resistance crisis is the challenge we have set for our company," said Theriault. "The potential impact on human health, animal health and food safety motivates our team to use innovation to its most beneficial outcome—healthier people, healthier animals, and a healthier planet."

1. Lin, D. M., Koskella, B. & Lin, H. C. *World J. Gastrointest. Pharmacol. Ther.* **8**, 162–173 (2017).

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