Phage Enzybiotics: Innovative weapons in the war against antimicrobial resistance

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Bacteriophages are specific viruses which can lyse bacteria cells through the production of specific proteins at the end of the phage lytic cycle to release new progenies. The holin protein forms pores in the cell membrane to allow passage for the endolysin enzyme to hydrolyze the peptidogycan in the cell wall, causing cell lysis of the bacteria. These lysin enzymes are potential antimicrobial alternatives which may help alleviate the global antimicrobial resistance problem, thus the term enzybiotics have been coined for them. Here we report some of our work on phage enzybiotics, using Endo88, a *Staphylococcus aureus* phage enzybiotic as a model for Gram-positive endolysins as well as LysPot, an enzybiotic targeting *Pseudomonas otitidis* as a model for Gram-negative endolysins. Both lysins have been cloned and expressed and its ability to inhibit bacteria growth confirmed through plate lysis assay and/or turbidity reduction assay. Endo88 is shown to be a wide-host range enzyme as it can lyse multiple staphylococcal species and even *Enterococcus faecalis* while LysPot is very specific, only lysing *P. otitidis* when the outer membrane is disrupted. Notably, this is slightly different from what has been reported in literature as Gram-positive endolysins are generally known to be more specific due to the presence of the cell-wall binding domain which is absent in most Gram-negative endolysins including LysPot. Interestingly, the holin from the *P. otitidis* phage has better antimicrobial activity compared to the endolysin including a wide host-range comprising both Gram-positive and Gram-negative bacteria. These studies underlie the potential of phage proteins as alternative antimicrobials in the war against antimicrobial resistance.