



The use of bacteriophage endolysins as antibacterial compounds

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The widespread use of antibiotics to eliminate pathogenic microorganisms is currently under pressure, due to the alarming emergence of antibiotic resistance. This has forced scientists to widen their scope in the search for alternatives, and has drawn the attention to bacteriophage (phage) as new bactericidal entities. Phages are viruses that highly specifically recognize and infect bacteria. After invasion and multiplication of the host, phage can turn lytic by hydrolyzing the host's cell wall, using (endo)lysins. Lysins are hydrolytic enzymes that generally consist of two domains: a catalytic domain (e.g. N-terminal) and a C-terminal cell binding domain (CBD) that binds to a specific sugar molecule on the cell wall. The idea of using lysins as stand-alone active compounds has only been considered since recently [1]. Several reports show that the external addition of lysins to Gram-positive pathogens (*Bacillus anthracis*, Streptococci) results in an effective *in vivo* elimination of the organism, similar to the extent whole phages would kill them [2]. This demonstrates that purified lysins from phages serve efficiently as antimicrobials.

The access to a range of lytic bacteriophages and new phage isolates active against several pathogens has allowed us to screen their genomes and select for endolysins. Some were heterologously produced and purified, showing a similar activity range as their corresponding phages. Moreover, we are currently isolating endolysins from phages active against Gram-negative bacteria and developing strategies to apply them directly, without the need of pretreatment of the host's outer membrane.

[1] Nelson, D., Loomis, L., Fischetti, V.A., Prevention and elimination of upper respiratory colonization of mice by group A streptococci by using a bacteriophage lytic enzyme, *Proc. Natl. Acad. Sci. U S A.* (2001) **98**:4107-4112.

[2] Schuch, R., Nelson, D., Fischetti, V.A., A bacteriolytic agent that detects and kills *Bacillus anthracis*. *Nature.* (2002) **418**: 884-889.