This abstract is to be considered for oral presentation

Bacteriophage depolymerases: evolutionary insights and antivirulence strategies against bacterial pathogens

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Abstract

To be able to enter and replicate in exopolysaccharide slime or capsule surrounded bacteria, bacteriophages (viruses of bacteria) have evolved the ability to overcome the exopolysaccharides structure by producing virion-associated proteins with polysaccharide depolymerization activities. We have isolated > 20 bacteriophages infecting several species of the *Acinetobacter baumannii-Acinetobacter calcoaceticus* complex and demonstrate that they encode depolymerase enzymes to specifically recognize bacterial capsular types as ligands for host adsorption (1). These enzymes are integrated at the bacteriophage tail spikes C-terminus, genes with high genetic plasticity to allow to recognition of a vast variability of polymorphic capsular K antigens of their hosts.

We also show that depolymerases are effective antimicrobial agents against multidrug resistant *A. baumannii*. Heterologously expressed enzymes were showed to be active in several environment conditions, are refractory to resistant development, are non-nontoxic to mammalian cells and most importantly, able to make *A. baumannii* fully susceptible to host complement effect. Depolymerases can strip bacterial cells from their capusles, which diminish the bacterial virulence and expose them to the host immune system. This innovative antimicrobial approach was already applied in i) *Galleria mellonella* caterpillar, ii) murine sepsis and iii) human serum (2, 3). A single intraperitoneal injection of 50 µg of depolymerase is able to protect 60% of mice from dead, with a significant reduction in the pro-inflammatory cytokine profile (3). Overall this work demonstrates the great diversity of bacteriophage depolymerases, their role in phage infection and evolution and their therapeutic properties as antivirulence drugs against capsulated bacteria.

References

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