OP21. Novel capsular depolymerases-based strategy to kill multidrug-resistant pathogenic bacteria

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Multidrug resistant pathogens represent one of the greatest threats to human health of the new millennium. ESKAPE bacterial pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and other *Enterobacteriaceae* species) are the leading group among these so-called superbugs, which rapidly acquire resistances to several (and sometimes all) available antibiotics and cause a variety of nosocomial infections (e.g. bacteraemia and wound infections).
Our research has been leading an innovative approach based on bacteriophage-derived enzymes (called capsular depolymerases) against *A. baumannii* (see video at ref 1). Previously, we found that some bacteriophages (i.e. viruses that specifically infect bacteria) acquired the ability to infect different Acinetobacter hosts through acquisition of different capsular depolymerases (2). These enzymes located at the bacteriophage tails bind and degrade specific bacterial capsules types (2). Recently, recombinantly expressed capsular depolymerases showed to be active in several environment conditions, non-nontoxic to mammalian cells and able to make *A. baumannii* fully susceptible to host complement effect, namely in i) *Galleria mellonella* caterpillar, ii) murine and iii) human serum models (3, 4). A single intraperitoneal injection of depolymerase protect 60% of mice from dead, with significant reduction of pro-inflammatory cytokine profile (4). We show that capsular depolymerases fit the new trend of antimicrobials needed, as they are highly specific, stable and refractory to resistance as they do not kill bacteria per se, instead they remove bacterial surface polysaccharides, diminishing bacterial virulence and exposing them to the host immune system. This innovative antimicrobial approach can be applied to other pathogenic bacteria.

References
(1) Oliveira H. 2019. Novel antimicrobial therapy with phage derived depolymerases.
Vídeo link: https://www.ceb.uminho.pt/Videos/Details/3114
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(4) Oliveira H et al 2019. An highly efficient anti-virulent depolymerase against multidrug-resistant A. baumannii capsule K2 in Galleria mellonella and murine models of sepsis. Applied and Environmental Microbiology.
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