Seeking a phage-based therapy to control otitis media

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Otitis media is a common paediatric infection of the middle ear and the most common reason for which systemic antibiotics are prescribed in children. *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* are the most frequent bacteria identified in the middle ear fluid of children with otitis media. Current oral antibiotic therapy might be ineffective in the treatment of biofilms involved in this condition and encourages selection of antimicrobial resistant bacteria, contributing to the frequent recurrence and/or chronicity of the disease. Thus, the development of novel and alternative strategies for the treatment of otitis media is needed. Bacteriophages and their derived enzymes have shown promising antimicrobial effects against infectious diseases and their use against *S. pneumoniae* has been addressed in a few studies, nonetheless no study reports the use of virulent phages or endolysins against *H. influenzae* and *M. catarrhalis*. Our aim is to develop a delivery system containing bacteriophages and/or derived enzymes for a targeted treatment of otitis media. To achieve this purpose, samples from the middle ear fluid of children with otitis media have been collected and the presence of the main otopathogens assessed by culture methods. To date, *S. pneumoniae* was the most frequent pathogen detected (44.1%), followed by *M. catarrhalis* (38.2%) and *H. influenzae* (14.7%). In these samples the presence of other bacterial species was also observed. In different attempts, using nasopharyngeal, middle ear fluid and wastewater treatment effluent samples, we were not able to isolate any virulent phage against clinical isolates of *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*. Novel endolysins with predicted amidase and muramidase activity were identified in the genome of a *S. pneumoniae* virulent phage and in a *H. influenzae* prophage, respectively. The endolysin of *S. pneumoniae* (MSlys) was successfully cloned and expressed in *Escherichia coli*, in contrast to the *H. influenzae* lysin, which was not possible to express. Preliminary results of MSlys antibacterial activity showed reductions of 3 logarithmic units of R6st cells within 2 hours, having potential to be used in the control of otitis media infections.