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Efficacy of phage-antibiotic combination therapy for the control of P. aeruginosa biofilms in vitro

Rodrigues, Ana Catarina; Pires, Diana P.; Sillankorva, Sanna; Azeredo, Joana

Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, Universidade do Minho

Pseudomonas aeruginosa is regarded a “phenomenon of bacterial resistance”. This gram negative bacterium is responsible for 65% of mortality in the hospitals all over the world and its prevalence can be a consequence of important reasons: intrinsic resistance determined by virulence factors; acquired resistance mechanisms that lead to a low susceptibility to antimicrobial agents; and the ability of P. aeruginosa to grow in any natural and artificial surfaces leading to the development of biofilms.

The emergence of new strategies to control P. aeruginosa biofilms is becoming more evident due to their resistance to traditional treatments and bacteriophages have been recognized as an attractive alternative for this problem. Nevertheless, despite the potential of phages as antimicrobial agents, it is well known that bacteria can quickly adapt and create new survival strategies and the emergence of phage-resistant phenotypes is inevitable. Thus, the combination of phage and antibiotic therapies could have potentially more benefits than just using phages and antibiotics alone.

This work describes the synergy between different P. aeruginosa phages (phiIBB-PAP21, phiIBB-PAP1, phiIBB-PAC23 and phiIBB-PAA2) and antibiotics (amikacin, ciprofloxacin, piperacillin and tetracycline) against planktonic cultures and biofilms. The efficacy of phages and antibiotics were evaluated by the enumeration of viable cells and the determination of biofilm biomass, or by the measurement of absorbance (OD600nm) in the case of planktonic cultures. In biofilms, the individual use of phage phiIBB-PAP21 and amikacin resulted in a reduction in the number of viable cells of 1.3 and 1.76 log, respectively, while the combination therapy of both resulted in approximately 3.66 log reduction. In the case of phages used together with ciprofloxacin the biofilm eradication was total. A possible explanation for this behaviour lies on the disruption of the biofilm matrix induced by some of the phages which can enhance the antibiotic penetration and availability to the cells. Nevertheless more studies are in progress to disclose this synergistic behaviour.