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PHAGE-HOST INTERACTION WITH CELLS IN DIFFERENT METABOLIC STATES: A S. *EPIDERMIDIS* CASE

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In nature, bacteria are not frequently found in the exponential state of growth. One particular issue is that the efficacy of antimicrobials, including phages, is always tested against bacterial cells at their highest growth rate. The majority of bacterial biomass occur in the form of a biofilm. Biofilms have a high tolerance to antimicrobial agents, mainly, due to the low metabolic activity of the biofilm cells and the presence of the biofilm matrix. To date, only a few staphylococcal phages were shown to be efficient against biofilms. In addition, there are only two reports of phages capable of successfully infecting cells in a low metabolic state. In this study, the *Staphylococcus epidermidis* phage SEP1 was used as a model to study phage-bacteria interactions. We demonstrated that besides some interesting features, this phage showed a reduced activity against biofilms. We clearly showed that the biofilm matrix was the main factor influencing SEP1 inefficacy against biofilms. In addition, SEP1 was shown to be highly effective against persister cells, biofilm-released cells and stationary-phase cells. This rare phenomenon was very recently studied through an RNA-seq analysis, where we demonstrate that SEP1 successfully hijacks the transcription machinery of its host, activating important metabolic and biosynthetic processes in stationary cells necessary for its effective replication. The gathered data provides important insights for a better implementation of phage therapy, since phages with ability to infect stationary cells could be more efficient in the treatment of patients with biofilm-related chronic infections.

KEYWORDS: bacteriophages; biofilms; stationary-phase cells; phage/bacteria interactions; RNA-seq

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