P303. The *Staphylococcus epidermidis* biofilm matrix confers protection against a phage that is highly active against dormant cells

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The complex biofilm structure confers to bacteria a key survival strategy. Biofilms are microbial communities that can attach to both abiotic and biotic surfaces and are frequently associated with the development of several nosocomial infections. The increasing need for innovative and efficient treatments to target these complex structures has led to an increasing interest on phages as a strategy for biofilm control and prevention. Theoretically, due to the closeness of cells, phage infection of biofilms is expected to be very efficient. However, several reports on phage-biofilm interactions had demonstrated a poor efficacy. In fact, the biofilm phenotype protects cells against phage predation due to several factors such as the dense involving matrix, cells with low metabolic rate and the quick development/multiplication of phage resistant variants. Staphylococci are amongst the most prevalent genera isolated from different types of infection. They usually form thick biofilms and are very difficult to target with antibiotics being, consequently, a useful model to study phage-biofilm interactions. Several staphylococcal phages were isolated and tested against biofilms. Although some studies have demonstrated the efficacy of phage against biofilms, only a few were successful against staphylococcal biofilms.

In this work we isolated a novel *Staphylococcus epidermidis*-specific phage, named SEP1. SEP1 has a broad lytic spectrum of activity and the rare ability to infect stationary phase cells. Indeed, phage-host interactions were analyzed by flow cytometry that showed that stationary-phase cells responded immediately to SEP1 addition. Moreover, quantitative PCR experiments revealed that phage genes were already being expressed after 5 minutes of contact with stationary phase cells.

However, SEP1 was inefficient against *S. epidermidis* biofilms. To understand the underlying factors impairing SEP1 inefficacy, this phage was tested against distinct biofilm-derived bacterial populations. Interestingly, SEP1 was able to lyse both active and dormant biofilm cells, suggesting that the inefficacy on biofilm control resulted from biofilm composition and architecture. To demonstrate this hypothesis, SEP1 was tested in scraped biofilms resulting in a 2-log reduction in the number of culturable cells, after six hours of infection. Our results provide compelling evidence indicating that the biofilm matrix can work as a decoy, hindering phage infection.