CONSIDER FOR TALK

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Phage Face Cream – Evaluation of Propionibacteriophage for Treatment of Acne Vulgaris and Discovery of Potential Superinfection and CRISPR Immunity Mechanism

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*Propionibacterium acnes* is a gram positive bacterium associated with acne vulgaris. Traditional antibiotic-based treatments have had limited success due to development of bacterial resistance. Phage therapy shows promise as an alternative in order to circumvent this issue. In order for *P. acnes* phage therapy to be effective, the phage must be able to infect acne-associated strains and successfully lyse target strains. In this study, two novel siphoviridae phages, Aquarius and Supernova, were isolated in order to investigate these questions. Host range assays were performed for both phages on a variety of clinical isolates of *P. acnes*. Supernova, which formed clear plaques, was able to infect acne-associated ribotype IV and V *P. acnes* strains and both Supernova and Aquarius were able to infect CRISPR-containing strains B66.8 and HL042PA3, respectively. BLASTn revealed mutations in protospacers known to confer phage-resistance to each of these strains. In light of its broad host range and capacity to infect acne-associated strains, Supernova was mixed with Cetaphil cream, a practical vehicle to deliver phages to the skin, and streaked on *P. acnes* lawns. The phage cream, even when stored for multiple days under different conditions, showed lysis of the surrounding bacteria, indicating that topical phage treatments may be a promising therapeutic delivery method. Interestingly, the host range assay for phage Aquarius was characterized by bacterial growth in the centers of areas of clearing. Previous studies have indicated that some *P. acnes* phages may have a pseudolysogenic life cycle, which is characterized as a circularized phage genome existing as an episome within the bacterial host. Based on this, it was hypothesized that Aquarius had a potential to be a pseudolysogenic phage. Bacteria were isolated from the center of clearings and characterized as pseudolysogens capable of releasing phage. Genome circularization was confirmed by PCR and genomic sequencing. The Aquarius pseudolysogens also demonstrated superinfection immunity upon reinfection with phage Aquarius. Genome annotation of Aquarius and Supernova revealed a putative conserved gene, gp41, which may contribute to this phenotype. A function for this protein has never been described for *P. acnes* phages, however, the protein prediction tool InterPro and the motif prediction tool MEME revealed a profoundly similar signature profile and two repeat motifs among gp41 and the lipoprotein of temperate phage (Ltp) TP-J34 (a *Streptoccocus thermophilus* infecting phage). This suggests that a superinfection immunity mechanism may be present in *P. acnes* phages that would prevent efficient bacterial lysis. In conclusion, despite the success of the phage cream, the results of the CRISPR and superinfection-resistance experiments suggested that these parameters must be addressed in future endeavors for efficacious application of *P. acnes* phage-based therapeutics.