Computational Analysis of the Cystic Fibrosis Lung Microbiome and Development of a Non-Toxic Quorum Quenching Cocktail Therapy To Inhibit Multispecies Biofilm Proliferation

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Bacterial biofilms account for 80% of all chronic microbial infections. ESKAPE pathogens form dense, multispecies biofilms that are resistant to most antibiotics. In this project, a combination treatment of FDA-approved concentrations of quorum quenching agents was devised to target three major interspecies biofilm-pathways: Chlorogenic Acid (CA) inhibiting Pseudomonas fluorescens-Staphylococcus epidermidis HQNO production by targeting Pqs Quorum Sensing (QS), carvacrol inhibiting P. fluorescens-Burkholderia pyrrocinia N-acyl-homoserine-lactone production by targeting Las QS, and 6-gingerol inhibiting P. fluorescens-Candida albicans phenazine production by targeting Rhl QS. Computational analysis of the cystic fibrosis lung microbiome using QIIME2 and PICRUSt2 confirmed the prevalence of these biofilm pathways. Docking analysis supported the binding affinities of each treatment with targeted enzymes (LasR/LasI/PqsR). Dual combinations of microbes were treated with 0.75% carvacrol, 30ug/ml CA, or 32ug/ml 6-gingerol, and the multispecies group was treated with all agents. Of the dual-species groups, CA had a 70% efficacy in inhibiting P. fluorescens-S. epidermidis biofilm, carvacrol a 60% efficacy on P. fluorescens-B. pyrrocinia biofilm, and 6-gingerol a 45% efficacy on P. fluorescens-C. albicans biofilm. The combination treatment demonstrated an 80% efficacy in inhibiting P. fluorescens-S. epidermidis-B. pyrrocinia-C. albicans biofilm. Statistical significance was confirmed using ANOVA and T-test. Treatment safety was supported by a cytotoxicity assay on A549 human alveolar epithelial cells. These findings support the delivery of the cocktail therapy as an adjuvant to antibiotics in-vivo, thus reducing morbidity and mortality from chronic biofilm-related infections.

Awards Won:
First Award of $5,000
Air Force Research Laboratory on behalf of the United States Air Force: Glass trophy and USAF medal for each recipient
Air Force Research Laboratory on behalf of the United States Air Force: First Award of $750 in each Regeneron ISEF Category