Cystic Fibrosis (CF) is a lethal inherited autosomal recessive disorder, which affects approximately 70,000 individuals worldwide. The disease is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR), which causes a malfunction in the chloride ion channel, and results in decreased volume of the periciliary fluid within the lower respiratory tract. This impaired function effects the epithelial cells of multiple organs, though, the lungs of CF patients are the biggest concern. The lungs are associated with the majority of the mortality and morbidity seen with the disease due to impaired mucociliary clearance, microbial infections, and chronic inflammation. The host will produce and recruit innate immune cells (e.g., neutrophils) to combat microbial infections, however, in CF patients, neutrophils are incapable of clearing such infections due to impaired effector function. Moreover, bacterial pathogens, such as Pseudomonas aeruginosa can adapt and persist due to their ability to produce biofilms and protect themselves against these host defense cells and antimicrobial components. Research is aimed to determine novel antimicrobial agents using a comprehensive proteomic study, to better characterize the outcome of the interactions between neutrophils and P. aeruginosa biofilms in CF. In this proposal, the differences in neutrophil composition between wild type and CF cell lines during P. aeruginosa infections will be analyzed to determine particular enzymes of interest. Following this, enzymes with altered production profiles between WT and CF cell lines will be investigated, to evaluate the ability of the enzymes to clear P. aeruginosa biofilms.