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Investigating *Mycobacterium smegmatis'*
Electron Transport Chain Through Use of Chemical Inhibitors

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*Mycobacterium tuberculosis* has infected approximately one out of every four people globally as reported by the CDC. One possible source for an antibiotic solution is the Electron Transport Chain. Using *M. smegmatis* as a model organism, I investigate the mycobacterial electron transport chain using known chemical inhibitors and identifying whether they have a specific target within the electron transport chain. Two oxidoreductases of interest include \( qcrB \) and \( cydA \). My current research involves work with the CWHM1023 (CB81-family) chemical inhibitor. It is hypothesized that this compound acts through targeted inhibition of the \( qcrB \) oxidoreductase. This hypothesis is based on prior experiments showing a decrease in ATP levels of *M. smegmatis* following exposure to CWHM1023, as well as the discovery of a mutation in \( qcrB \), QcrB\(^{A178T} \), conferring resistance to CWHM1023. In an effort to confirm this hypothesis, various deletion mutants of \( qcrB \) and \( cydA \) in *M. smegmatis* have been constructed using novel phage recombineering methods. These mutants are then complemented with either empty vector, the original deletion, or a mutant version of the deleted sequence (QcrBA\(^{A178T} \)) in an effort to confirm with certainty the targets of CWHM1023. To test the effects of CWHM1023 on the various strains, I utilize the Microplate Alamar Blue Assay (MABA), which tests for respiration levels of bacteria through quantification of the reduction of blue-colored Resazurin to the pink Resorufin. Numerous MABA experiments have thus far been conducted, and have provided promising data supporting \( qcrB \) as the target of CWHM1023. However, current research directions involve cloning of new complement strains that account for possible genetic polar effects given the existence of \( qcrB \) and \( CydA \) in operons. Confirmation of \( qcrB \) as the target of CWHM1023 will provide novel understanding of the organization of the mycobacterial electron transport chain, and ways by which it may be inhibited.