Developing Novel Protein Targets for Bordetella pertussis Antibiotics: Understanding Protein Interfaces and Domain-Domain Interactions

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Biofilms infections show increased antibiotic resistance thus necessitating the search for novel therapeutics. Bordetella pertussis biofilm infections, or whooping cough, have resurged globally because of lowered vaccine rates and new strains of whooping cough. The purpose of this project was to identify key targets of BpeGReg, a protein shown to cause B. pertussis biofilms, that would further the development of those therapeutics. Previously, only the H225 residue of BpeGReg had been researched; everything else about this protein remained unknown. By utilizing HPLC activity, protein-protein interaction pull down assays, and native gels, it was found that the middle domain interacted with the full-length protein. This middle domain interaction has great potential for controlling oligomerization states. Given that BpeGReg needs to be in a dimer form to be active, peptides simulating the interacting surface of the middle domain could be used to prevent c-di-GMP formation and thus inhibit biofilm formation. This research establishes vital targets of future B.pertussis treatment through the ability to modulate oligomerization states and target heme pocket oxygen-binding.

Awards Won:
Second Award of $2,000