Changes in Amino Acid Sequence that Confers Functionality of Heme-Iron Transport Proteins in Haemophilus influenzae

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Nontypeable Haemophilus influenzae (NTHI) is a commensal, gram-negative bacterium that colonizes the human nasopharynx. Additionally, NTHI has the capacity to become pathogenic and is a known causative agent in both lower and upper respiratory tract infections. In adults and children, NTHI is involved in otitis media (OM), sinusitis, exacerbations of chronic obstructive pulmonary disease (COPD) and cystic fibrosis. The sequestration of nutritional elements, including heme-iron, in hosts is a defense against the growth of bacteria. Despite these obstacles, NTHI employs several mechanisms to optimize the utilization of heme from heme sequestering complexes within the host. NTHI has developed a series of overlapping mechanisms that transport proteins across both the periplasmic and cytoplasmic membranes. Several proteins have been previously identified as involved in this process. In this study, I investigated the contribution of HxuA, Hup, and HbpA to heme-iron transport. I initially analyzed the genes of 22 clinical isolates from patients with OM and 10 clinical isolates from patients with early and late term COPD. Genomic sequencing revealed both variation and conservation of amino acid sequences of each protein across all clinical isolates investigated. To evaluate the functionality of these genes, I constructed a mutant that lacked hup and determined its growth with heme as the sole iron/heme source. I hypothesize that this, and future, mutants will help provide insight into heme-iron utilization by NTHI in the host and the use of these proteins as effective therapeutic targets for treatment of NTHI diseases.