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IDENTIFICATION OF VIRULENCE FACTORS IN INVASIVE *HAEMOPHILUS INFLUENZAE* ISOLATES CAUSING DISEASE IN UTAH CHILDREN

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Abstract

Haemophilus influenzae can cause serious disease in children. After widespread use of the *H. influenzae* serotype b (Hib) vaccine, *H. influenzae* serotype a (Hia) became a significant cause of invasive infection in Utah. Although most Utah Hia isolates belong to a sequence type theorized to be less invasive, disease is severe and clinically similar to Hib. In this project, I describe clinical characteristics of invasive Hia in Utah and identification of genes involved in adhesion and branched-chain amino acid biosynthesis that may contribute to the unique virulent nature of the Utah Hia strains. For my research, I focused on three different lines of investigation related to this topic: clinical and molecular epidemiology of the Hia isolates in Utah, the phylogenetics and virulence factors associated with them and a case series of neonatal early onset sepsis caused by *H. influenzae*, an uncommon pathogen in this disease.

Investigation of the unique epidemiology of Hia isolates causing invasive disease in Utah children showed that while our disease was severe, with clinical presentations and outcomes similar to disease caused by Hib and Hia strains in previous literature, our strains belonged to the uncommon sequence type 62 (ST 62), which is part of phylogenetic division II and thus theoretically less virulent. Sequencing analysis focused on the known capsule duplication-deletion found in Hib and some Hia strains that leads to increased capsule production. None of the isolates contained the duplication deletion even though the disease outcomes were severe. Our ST 62 isolates were found to be more genetically similar to each other and to *H. influenzae* serotype f (Hif) than to Hib and non-ST 62 Hia isolates. Analysis of virulence genes of our Hia isolates like adhesion genes *oapA* and *yadA*, and the BCAA biosynthesis gene *ilvGM*, found allelic variation possibly associated with phase switching. We also identified ten neonates who had early-onset sepsis caused by *H. influenzae*.