JURA
Journal of Undergraduate Research in Alberta

UNIVERSITY OF CALGARY

# INVESTIGATING THE SEQUENCE DIVERSITY OF TRANSFERRIN BINDING PROTEIN B IN HAEMOPHILUS INFLUENZAE

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## INTRODUCTION

*Haemophilus influenzae* (*Hi*) is a Gram-negative bacterium that is exclusive to the upper respiratory tract of humans. *Hi* strains possessing an extracellular polysaccharide capsule, particularly serotype b *H. influenzae* (*Hib*), are responsible for invasive infections such as bacterial meningitis and bacteremia. Strains without a polysaccharide capsule, known as non-typable *H. influenzae* (*NTHi*), are responsible for ear infections and other diseases in children. Disease caused by *Hib* infections has become rare in developed countries since the introduction of a conjugate serogroup b vaccine. However disease caused by *NTHi* and other *Hi* serotypes, particularly type a *Hi*, has increased [1]. To prevent disease caused by non-vaccine *Hi* serotypes novel vaccines will need to be produced that are effective against multiple serotypes of *Hi*, including *NTHi*

It has been demonstrated that transferrin binding protein B (TbpB) in the porcine pathogen, *Actinobacillus pleuropneumoniae (Ap)*, is essential for survival and causing disease in a porcine infection model [2]. TbpB is now being developed as a vaccine target. Since *Ap* and *Hi* are both host-restricted bacteria in the Pasteurellaceae family, we consider TbpB in *Hi* as a logical vaccine target. .

## METHODS

To investigate the diversity of TbpBs in *Hi*, the *tbpB* genes from a collection of 43 unique *Hi* strains from Canada, the United States and England were sequenced. These strains represent a wide diversity of clinical manifestations and serotypes, allowing us to investigate the diversity of the *tbpB* gene in *Hi*. Phylogenetic analysis was undertaken to cluster the *tbpB* genes based on sequence similarity. These analyses of the relationships between phylogenetic clusters and clinical/epidemiological information explore the prevalence and diversity of transferrin receptor genes in *Hi.*

## RESULTS

Analysis of the data showed that the sequences of the various TbpB proteins clustered independently of serotype. This shows that development of a TbpB-based vaccine would logically target all serotypes and non-typeable strains, rather than having to develop a series of vaccines for the different groups. The analysis of the multiple sequence alignments generated from the TbpB sequences showed higher conservation in the C lobe of TbpB than the N lobe. Of particular interest was the observation made while mapping conserved regions of the sequence alignments to a structural model of TbpB that a region exists on the N lobe of TbpB which is highly conserved in all *Hi* strains sequenced.

## DISCUSSION AND CONCLUSIONS

The immunogenic properties of this conserved region of TbpB have not yet been investigated. The number of strains sequenced was also limited and they were only of serotype B and *NTHi*. More diverse *Hi* strains need to be sequenced to confirm the conservation of TbpB across all serotypes and further studies still need to be completed to confirm that these conserved regions are actually immunogenic. However this study has shown that TbpB has potential to be used as a target for a new cross protective *Hi* vaccine.

## REFERENCES

1. Rubach, M et al. Emerg Infect Dis. **17**: 1645-1650, 2011.
2. Balts, N et al. FEMS Microbiol Lett. **209**: 283-287, 2002