ABSTRACT

Burkholderia pseudomallei (Bp) is a motile gram-negative bacillus and causative agent of the febrile disease melioidosis. Bp is an opportunist bacterium with diabetes mellitus as a major risk factor. Bp can evade clearance by the alternative pathway of the complement cascade enabling it to invade cells and persist intracellularly. Factor H (fH) is a negative regulator of the alternative pathway which protects host surfaces. Several microbial species are known to mimic host surfaces or deceive fH self-recognition domains by binding via a fH binding protein (fHbp). Bacteria with the ability to bind fH to their surface include *Yersinia enterocolitica*, via adhesin YadA, *Neisseria meningitidis* via fHbp and H*aemophilus influenza* via P5.

This study used *in silico* and *in vitro* methods to investigate the ability of Bp to bind to host complement regulatory protein factor H. *In vitro* studies found that Bp can bind host complement regulatory protein fH on its surface via one or more proteins with a molecular weight of approximately 37kDa. Candidate fHbps OmpA and Omp38 were recognized by mass spectrometry analysis.

BLAST database searches identified OmpA and BpaC as candidate fHbps. Topological algorithms speculated BpaC and OmpA to be partially extracellularly exposed on the bacterial surface. Rigid-body docking methods characterized conformations in which OmpA and BpaC would interact with fH domains 19-20. Binding affinities between BpaC and OmpA bound to fH domains 19-20 was predicted to be stronger than the interaction between known fHbp *Borrelia burgdorferi* OspE and fH domains 19-20.

A direct interaction between fH and the recombinant versions of candidate fHbps Omp38 and OmpA has not yet been confirmed using molecular biology methods. *In vitro* methods to investigate the BpaC and fH interaction are still to be explored. The identification of Bp proteins that bind to fH will provide a therapeutic target which may have potential as vaccine candidates to be used towards reducing the global burden of melioidosis.

THESIS COMMITTEE

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THESIS PRESENTATION
by
Caroline Lambert

August 1st, 2018

"The identification and description of *Burkholderia pseudomallei* proteins that bind host complement-regulatory proteins via *in silico* and *in vitro* analyses"

M.S. in Biomedical Sciences

HONORS

Nominated to attend University of Toledo Advanced Leadership Academy, 2018.

Satellites Auxiliary Volunteers of UT-HSC Scholarship-in-need awardee, 2018.

FUTURE PLANS

Caroline plans to return to England and pursue a job in bioinformatics.

PRESENTED ABSTRACTS

C. Lambert, L. Stanbery, I. Syed, R.M. Wooten, The identification and description of *Burkholderia pseudomallei* proteins that bind host complement-regulatory proteins via *in silico* and in *vitro* analyses.

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Graduate Research Forum,

University of Toledo Health Sciences Campus, March 2018, Toledo, Ohio.

Midwest Graduate Research Symposium, University of Toledo Main Campus, April 2018, Toledo, Ohio.

Intelligent Systems for Molecular Biology Conference, Hyatt Regency Hotel, July 2018, Chicago, Illinois.

PUBLICATIONS

C. Lambert (June, 2018) UT researchers use 'in silico' approach to study diseases, The Toledo Blade.