Assessing the abilities of Factor H-Fc IgG fusion protein variants as a therapeutic against *Burkholderia pseudomallei*

Hugo Sigona Gonzalez[1], Kelly Morgan[1], R. Mark Wooten, PhD[2]

[1]College of Medicine and Life Sciences, The University of Toledo, Toledo, Ohio 43614
[2]Department of Medical Microbiology and Immunology, The University of Toledo, Toledo, Ohio 43614

*Corresponding author: Hugo.SigonaGonzalez@rockets.utoledo.edu

Published: 22 May 2024

Introduction: *Burkholderia pseudomallei* (Bp) is a Gram-Negative bacterium and is emerging as a global health threat, including the America's, causing melioidosis and lethal sepsis. Because Bp has a $LD_{50} \geq$organisms, it is designated as a Tier 1 select agent due to its bioweapon potential. Bp is naturally resistant to most antibiotics and there is no vaccine, thus there is a great need for therapeutics.

Methods: One of Bp's important virulence mechanisms is its ability to evade the host complement system. We have identified a surface protein expressed by Bp that can bind host Factor H, which is a negative regulator of the complement cascade and thus promotes immune evasion. Focusing on this mechanism, we are collaborating with Planet Biotech which has generated several chimeric molecules which contain the host binding site for Factor H and the other portion consists of the Fc region of human immunoglobulin G. Thus, this chimera should competitively bind to the bacterial surface, eliminating their ability to bind functional Factor H, and the IgG Fc region should activate the complement cascade to mediate direct and/or opsonophagocytic killing by immune cells.

Results: Our preliminary studies indicate that a subset of the initial constructs were able to bind to Bp, initiate C3 deposition, and generate membrane attack complexes (MAC) on their surface using ELISA. Based on these findings, we are now testing a second generation of constructs. Our current findings indicate that a subset of these new constructs are able to bind to, elicit C3 deposition, and generate MAC on Bp's surface better than the original construct. These chimera's are also able to promote direct killing of Bp strains.

Conclusion: Future studies will test their ability to promote opsonophagocytic killing by neutrophil/macrophages and protect mice from challenge with Bp.

Funding Acknowledgement:

NIAID: AI121970; DoD: W81XWH-21-TBDRP-IDA, #13193455

