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Grant Title: A toolbox to discriminate functionally important glycan receptors for virulence

Abstract

Glycoconjugates are positioned at the functional interface between hosts and microbes. Many bacterial pathogens of public health importance translocate protein toxins during infection, a process that plays an essential role in virulence. In particular, bacterial AB_5 toxins, which consist of an enzymatic 'A' subunit(s) and a homopentamer of glycan receptor-binding 'B' subunit, play a crucial role in their acute and chronic stages of infection. Valuable tools such as glycan microarrays and lectins serve as the workhorse for determining the glycan-binding specificity of bacterial toxins, but they have limitations in further discriminating a glycan receptor(s) of physiological significance. Establishing a toolbox of customized, genetically engineered host cell lines can help overcome this limitation by discriminating functionally important glycan binder(s) in toxin-mediated virulence during bacterial infection. In this study, we generated knockdown cells of human intestinal epithelial cells and HEK293T cells possessing an impaired α2-3 sialosides biosynthesis. Using these cells, we show that the PltB subunit of each toxin exhibits different glycan-binding preferences that correlate with glycan expression profiles of host cells targeted by each bacteria at the primary infection or intoxication sites.