Host-specific Binding of ClfB in Staphylococcal Nasal Carriage

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Staphylococcus aureus nasal carriage is a state of subclinical bacterial harboring associated with threefold increased infection risk for ~25% of the healthy human population. The first stage of this study identified a novel pattern of host-specific binding of staphylococal adhesin ClfB to mammalial fibrinogen. In the second stage, phylogenetic reconstruction, whole-genome sequencing, and cell binding assays were used to further elucidate the evolutionary patterns of ClfB and to isolate and understand secondary adhesin IsdA. Maximum likelihood phylogenetic reconstruction showed congruent evolutionary topologies to maximum parsimony methods from Year 1. Loricrin binding assays showed WT S. lentus with greater adherence to mouse molecules than S. lentus ClfB- and WT S. aureus USA300 ($p<0.0001$), demonstrating host-specific divergence in the binding region of ClfB. A major setback for S. aureus research is the ineffective binding of human commensal S. aureus to WT rodents. Ineffective model systems pose a particularly large problem in developing vaccines and immunizations, prospective alternatives to the few effective antibiotic regimens that remain. Thus, a new tripartite cloning plan was conceptualized to engineer a S. aureus strain that expresses the more mouse loricrin-adherent ClfB binding region of S. lentus. Taken together, this study highlights the importance of considering host attachment tropisms in the design of individualized, preventative medical intervention.

Awards Won:
Second Award of $2,000