Investigation of a Novel Slam Dependent Heme Acquisition System in the Bacterial Pathogen *Acinetobacter baumannii*

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The Moraes lab recently discovered an Outer Membrane (OM) protein called Surface Lipoprotein Assembly Modulator (Slam) that is involved in the translocation of lipoproteins to the cell surface of the human pathogen, *Neisseria meningitidis*. These surface exposed lipoproteins (SLPs) are tethered to the OM by a lipid anchor, and play key roles as virulence factors, facilitating nutrient acquisition, and host colonization and immune evasion. Furthermore, a Slam knockout results in an avirulent Neisserial strain by preventing SLPs from getting to the cell surface.

Slams can be found in a variety of medically relevant, Gram-negative pathogens. One example is *Acinetobacter baumannii*, which is an opportunistic human pathogen that causes disease primarily in a hospital setting. Clinical manifestations include pneumonia and blood stream infections. Through bioinformatics, we discovered a Slam homolog (Slam X) within a mis-annotated *A. baumannii* gene cluster. This gene cluster also contains a predicted SLP of unknown function (SLP X), a heme oxygenase (degrades heme and liberates iron), and a TonB dependent OM transporter (TBDT), which imports limiting nutrients across the OM in bacteria. My hypothesis is that the gene cluster functions as a heme uptake system. Slam X translocates SLP X to the cell surface, where it functions to capture heme so it can be imported into the cell through the TBDT.

To date, I have confirmed that the lipoprotein is surface exposed in a Slam dependent manner. The structure of the lipoprotein determined by X-ray crystallography reveals a heme-binding site containing two critical Histidine residues, H33 and H96, involved in heme coordination. Binding experiments suggest that SLP X has a high affinity for heme, and can acquire heme from the host hemoprotein, hemoglobin. Preliminary growth assay results point to a role of the Slam gene cluster in heme uptake. Studying this novel nutrient acquisition system will shed light on an unexplored area of *A. baumannii* biology, and this information can be exploited for applied strategies to combat multi-drug resistant *A. baumannii* via specific antibiotics or vaccines.