

Poster #20**Jessica King****Post-Doc/Fellow, College of Medicine****Microbiology****Title of Research:** Staphylococcus Aureus Superantigens Promote Infective Endocarditis: Possible Contribution of Direct Interaction with Endothelial Cells**Other Authors:** Jessica King, Wilmara Salgado-Pabón**Introduction/Purpose:**

Infective endocarditis (IE) is described as an infection of the endocardial surface of the heart and is often characterized by the appearance of small growths called vegetations. Staphylococcus aureus is the leading cause of IE around the world. In the U.S. there are approximately 100,000 cases of IE yearly, with 40,000 of these cases being caused by S. aureus. S. aureus IE is an acute infection that often leads to severe clinical manifestations and poor patient outcomes including a high frequency of strokes, metastatic infections, and septic shock. Superantigens (SAGs) are critical contributors to the high rates of morbidity and mortality associated with S. aureus IE, and contribute to S. aureus colonization of damaged heart valves and/or persistence and growth of vegetations. SAGs bypass the normal antigen presentation pathway of immune cells by cross-linking the V β chain of the T-cell receptor (TCR) to the MHC II molecule on antigen presenting cells, inducing a powerful activation of both T-cells and macrophages with massive production of cytokines. A little-known fact is that SAGs can also interact directly with non-immune cells such as epithelial and endothelial cells and induce cytokine production by these cell types. Data show that making specific amino acid substitutions in the SAG dodecapeptide (ddp) region, a stretch of twelve amino acids located on the central alpha helix of the SAG molecule, inhibits cytokine release by human vaginal epithelial cells and fails to induce toxic shock in a rabbit model of menstrual toxic shock syndrome. We hypothesize that the ddp region is required for SAG interaction with the vascular endothelium, induction of persistence/chronic inflammation, recruitment of immune cells, and enhancement of vegetation growth.

Experimental Design:

We are testing this hypothesis in vitro using immortalized human aortic endothelial cells, and in vivo using the rabbit model of IE and sepsis.

Results:

In progress.

Conclusions:

In progress.