**Title:** *The impacts of alcohol-associated intestinal dysbiosis on pulmonary host defense and immune activation***.**

**Abstract**: Alcohol consumption perturbs the normal intestinal microbial communities. To investigate the impact of alcohol-mediated dysbiosis on immune activation and host defense we developed an alcohol-dysbiosis fecal adoptive transfer model, and two *ex-vivo* stimulation assays utilizing alcohol-dysbiosis associated microbiota products. We hypothesized that alcohol-mediated dysbiosis would increase susceptibility to *Klebsiella* pneumonia. We further hypothesized that microbial products produced by the dysbiotic alcohol-associated community would increase immune activation and intestinal permeability. First, mice were treated with a cocktail of antibiotics daily for two weeks. Microbiota-depleted mice were then recolonized by gavage with intestinal microbiota from alcohol-fed or pair-fed animals. Following recolonization groups of mice were sacrificed prior to and 48 hr. post respiratory infection with *Klebsiella pneumoniae*. We then assessed *Klebsiella* burden, lung immunology, and intestinal barrier damage and immunology. We found that mice recolonized with an alcohol-dysbiotic microbiota had increased pulmonary *Klebsiella* burden compared to mice recolonized with a pair-fed microbiota. Alcohol-dysbiotic microbiota recolonized mice also had increased intestinal damage as measured by increased levels of serum intestinal fatty acid binding protein. We also found that mice recolonized with an alcohol-dysbiotic microbiota had increased numbers of activated T-cells in the intestinal tract prior to and following *Klebsiella* infection, which is in contradistinction to the lungs of alcohol-dysbiotic microbiota recolonized mice both prior to and following *Klebsiella* infection. We then determined the impact of intestinal microbial products on immune activation and intestinal permeability. Fecal samples from alcohol- and pair-fed mice were cultured in Gifu Anaerobic Broth for 24 hours under anaerobic conditions. Live/whole organisms were removed and microbial products were collected and added to peripheral blood mononuclear cells (PBMC) or C2BBe1 intestinal epithelial monolayers. Following stimulation, immune activation of PBMC was assessed via flow cytometry and transepithelial electrical resistance (TEER) was measured using a volt/ohm meter. Microbial products from alcohol-fed mice significantly increased the immune activation (% of cells which express CD38) of CD4 and CD8 T-cells. Conversely, microbial products from alcohol-fed mice significantly decreased TEER compared to microbial products from control mice. Collectively, these data indicate that alcohol-dysbiosis is associated with; (a) increased pulmonary bacterial burden, (b) intestinal damage and inflammation, (c) intestinal T-cell activation, and (d) intestinal T-cell sequestration. In addition, our results indicate that alcohol-associated microbial products contribute to immune activation and intestinal permeability. Our findings also suggest that the gut-lung axis may be a potential mechanistic pathway involved in host defense against *Klebsiella* pneumonia.

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**Short Bio:** I graduated from Montana State University with a B.Sc. in microbiology. I then joined the laboratory of Dr. Konkel in 2009 at Washington State University for my graduate studies. After completion of my graduate work I joined the laboratory of Drs. Shellito and Welsh at Louisiana State University Health Science Center New Orleans as a postdoctoral researcher. During my time as a postdoctoral researcher at LSUHSC, I was fortunate to become a LA CaTS Meritorious Postdoctoral Scholar, which is funded through the Louisiana Clinical and Translational Science Center (Louisiana IDeA-CTR). This award also allowed me to successfully obtain an NIH funded K99/R00 Pathway to Independence Award. My research interests are in microbiology, host-pathogen interactions, and immunology. My research began with the study of the skin-resident bacterial flora found on mice and transitioned to the study of bacterial-host interactions of *Campylobacter jejuni* with a focus on the identification and characterization of *C. jejuni* virulence factors. Currently, my research is focused on determining the mechanisms by which alcohol-induced intestinal dysbiosis impairs pulmonary host defense against *Klebsiella* pneumonia.