Alcohol consumption, both acute and chronic, has diverse and well-documented effects on the human immune system. Melioidosis is an emerging infectious disease caused by *Burkholderia pseudomallei* of global public health importance, and a potential bioterror agent. Evidence suggests that binge alcohol consumption is a risk factor for the development of melioidosis. However, no experimental studies have investigated the effects of binge alcohol intoxication on *Burkholderia* spp. *in vivo* and the innate immune response during infection. The goal was to establish an animal model of alcohol and *Burkholderia* infection. We hypothesized that binge alcohol consumption will increase bacterial tissue dissemination by lowering innate immune mechanisms.

In this study, we used the close genetic *B. pseudomallei* relative *B. thailandensis* E264 as a useful BSL-1 model system to study the effects of binge alcohol consumption during a *Burkholderia* infection. Eight-week-old female C57BL/6 mice were administered alcohol comparable to human binge drinking episodes (4 g/kg) or PBS intraperitoneally 30 min before a non-lethal intranasal infection with $1 \times 10^5$ *B. thailandensis* CFU. Animals were euthanized at 24 and 72 hr post infection (PI): blood and tissues were collected to determine bacterial load and dissemination. At 24 hr PI, bacteria accumulated in the lung and disseminated to the liver, and spleen, in alcohol treated mice compared with no tissue burden within the control-no alcohol treatment group. In addition, the greatest bacterial load occurred in the spleen of alcohol-administered mice compared to control. At 72 hr PI, bacteria had persisted and replicated beyond the initial bacterial dose in the lungs and the brains of alcohol-administered mice. Cumulatively, this tissue accumulation of *B. thailandensis* suggests that alcohol treatment increases the potential for bacterial dissemination with only 30 min of alcohol treatment. Cytokine and chemokine values were decreased in serum from alcohol groups as well as tissue (lung, spleen) concentrations of cytokines (TNF-a, GM-CSF, IL-10) compared to *B. thailandensis* infection alone without alcohol treatment. Increases in lung and brain permeability barriers were observed as early as 2.5 hr. post alcohol administration based on the intravenous injection of Evans Blue dye. A transepithelial/endothelial electrical resistance (TEER) assay was used to measure the effect of binge alcohol levels on murine lung epithelial (EphH4) and brain endothelial (bEnd.3) monolayers. TEER was significantly decreased with (22mM and 50mM) alcohol exposure after 1 hr. These results and our previous macrophage studies suggest that binge alcohol consumption may suppress immune signaling and increase the ability of a low virulence strain to go systemic through increases in barrier permeability. In addition, this mouse data supports the finding that alcohol consumption is a predisposing factor for melioidosis. Future research will investigate the mechanism of tissue tight junction dysfunction for bacterial dissemination during binge alcohol episodes and how an increase of blood alcohol levels effect a higher pathogenic *B. pseudomallei* isolate and melioidosis rates of infection.