**BACKGROUND**

- Chronic immune activation and persistence of viral reservoirs remains a challenge for achieving complete immune recovery and viral eradication in Human Immunodeficiency Virus (HIV) infected patients. Simian Immunodeficiency Virus (SIV) infected rhesus macaques provide an excellent nonhuman primate model that manifest clinical, immunologic, and pathologic changes similar to that in human HIV infection.
- HIV infection driven CD4+ T cell depletion is progressive in peripheral blood, but rapid and severe in gut associated lymphoid tissue (GALT), leading to impaired mucosal immunity, gut epithelial barrier disruption, and viral persistence.
- Pilot studies have shown that probiotic bacteria provide reversal of CD4+ T cell loss, inflammation, and metabolic symptoms associated with infection.
- Using a novel ligated intestinal loop model in SIV-infected rhesus macaques, we have investigated the impact of probiotic microbes on inflamed gut mucosa through the molecular signatures of immune function in combination with histopathological changes in the gut epithelium.

**OBJECTIVES**

1. To characterize the pathogenic effects of chronic SIV infection (10 weeks) on the in vivo mucosal immune function in rhesus macaques in comparison to uninfected controls
2. To investigate the in vivo gut mucosal responses to commensal bacteria (Lactobacillus plantarum and Bifidobacterium infantis) using the ligated ileal loop model in SIV-infected macaques and negative controls

**METHODS AND MATERIALS**

**Ligated ileal loop model:**

- 4 SIV (-) animals
- 4 SIV (+) animals

**Analysis:**

- Fluorescence microscopy
- Real-time PCR
- Immunochemistry
- Microbiome analysis

**RESULTS**

- SIV infection induced a marked inflammatory response in the gut mucosa, causing immune and epithelial disruption.
- Probiotic bacteria *L. plantarum (LP)* and *B. infantis (BI)* both suppressed inflammatory cytokine and chemokine expression in SIV-infected gut.
- *L. plantarum* rapidly reverses epithelial barrier damage in SIV infected gut within 5 hours

**SUMMARY AND CONCLUSIONS**

- To our knowledge, ZO-1 or other epithelial tight junction proteins in intestinal epithelium have never before been investigated and quantified based on 3-D structure at such resolution.
- Chronic SIV infection causes dramatic upregulation of inflammatory genes and IL-18 signaling, leading to disruption of epithelial barrier.
- Probiotic bacteria suppress inflammation and reverse damage associated with SIV infection, suggesting the critical role of the synergistic host-microbiota relationship in chronic disease.

**REFERENCES AND ACKNOWLEDGEMENT**

Acknowledgements:
- UC Davis Students for Advanced Research program, NIH T35, UC Davis Veterinary Scientist Training Program

References: