Host-Commensal Dynamics in HIV Infection

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It's estimated that the gastrointestinal tract (GIT) is home to 100 trillion bacteria. These commensal, organisms help us to absorb nutrients from food, prevent colonization by pathogenic bacteria, and maintain the function of our GI immune response. Increasing evidence supports the idea these commensal bacteria play a critical role in the maintaining our GIT by a crosstalk of signals to the gut epithelial barrier and the mucosal immune system. However, inflammation can disrupt this crosstalk leading to GI complications.

The GIT is severely damaged by Human Immunodeficiency Virus (HIV). The rapid depletion of CD4 T cells, damage to the epithelial barrier, and changes to microbial composition of the GIT is observed in HIV infection. As HIV infection progresses the defects in the GIT results in the translocation of bacteria or bacterial products from the gut into the systemic circulation. In addition, the depletion of CD4 T cells leads to an increase in opportunistic infections in chronic HIV infection. Some commensal bacteria have probiotic properties that can help improve the condition of the GIT. Lactobacillus plantarum (L. plantarum) is a commensal bacteria that is known to dampen inflammatory responses as well as strengthen the integrity of the epithelial barrier. This has lead to clinical trials involving the treatment of HIV patients with probiotic therapies. However, whether probiotics are able to function normally in chronically infected patients due to changes in the bacteria or in the host and how it perceives the signals from the bacteria.

In this study we test the idea that SIV infection causes an inflammatory environment in the GIT. As a result, commensal bacteria may change their gene expression profiles in response to the inflamed environment. In addition we hypothesize that the signaling pathways that are involved in the host-commensal crosstalk is modified such that there is a loss of the beneficial effects of L. plantarum in chronic HIV infection. To accomplish this we will be using the Simian Immunodeficiency Virus (SIV) model of HIV infection. We will inject L. plantarum into the small intestine of SIV infected rhesus macaques and then retrieve the intestinal content after five hours to sequence the changes in gene expression by the bacteria. We will also take gut samples to look at the protein expression of various components of the signaling pathways that are utilized when L. plantarum interacts with the host. This study presents an opportunity to understand how the relationship between the GIT and commensal bacteria changes with HIV infection. By identifying the defects, we can start to develop therapies that can restore the host-commensal relationship and repair the GIT.