Title: Immune activation is associated with specific gut microbes in people living with HIV

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For people living with HIV (PLWH), antiretroviral therapy (ART) has been shown to control viral replication resulting in undetectable plasma viral load levels. However, despite ART, chronic inflammation and immune activation (IA) are continued predictors for mortality in PLWH due to increased risk of inflammation-mediated conditions. Damage to the gut mucosa from HIV infection, and subsequent translocation of microbial products such as lipopolysaccharides, have implicated the gut microbiome as a potential mediator of chronic inflammation and IA in PLWH. In addition, specific strains of gut bacteria have been shown to activate CD4+ T cells, which is a potential mechanism for chronic IA. To investigate the role of the gut microbiome in IA, we are enrolling 70 patients infected with HIV that are currently on ART from 3 study sites (located in Minnesota and Mexico City) and are collecting gut biopsies, stool, plasma, and clinical lab measures (i.e., CD4+ and CD8+ T cell counts). In a preliminary analysis, we performed 16S rRNA sequencing on ileum, rectum and stool samples from 12 patients in Minnesota categorized as either immunological “Responders” or “Nonresponders” based on their CD4+/CD8+ T cell ratios (<0.52 for Nonresponders, >1.08 for Responders). Differential abundance analysis showed that Nonresponders had significantly different relative abundance of several microbes, including higher Subdoligranulum in the rectum and ileum biopsies ($p=0.06$ and $p=0.005$ respectively). Furthermore, the relative abundance of Subdoligranulum in rectum and ileum biopsies negatively correlated with CD4+/CD8+ ratios (Spearman correlation, $p=0.001$ and $p=0.048$ respectively). In addition to this analysis, we are currently quantifying concentrations of inflammatory cytokine and biomarker concentrations (e.g., IL-6, TNF, LBP, CRP) in matching plasma samples and sequencing gut biopsies from 40 additional patients to better integrate microbiome and inflammation data in PLWH. These results highlight the important role of the gut microbiome in IA in PLWH.