GUT BARRIER INTEGRITY AND MICROBIOTA IN HIV PATIENTS RECEIVING ORAL BACTERIOTHERAPY

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BACKGROUND

A direct association between enteric microbiota, intestinal homeostasis and inflammation during HIV-1 infection has been reported by lots of studies. People living with HIV-1 are characterized by a severe enteropathy, represented by a commensal bacteria translocation from gut to the bloodstream and a chronic immune activation, not repaired by the various therapeutic regimens. Several *in vitro* studies demonstrated that the direct interaction of HIV-1 with the apical surface of intestinal cells disrupts tight junction structures, which are critical for the morphological and physiological maintenance of mucosal epithelia integrity.

METHODS

Gut biopsies and fecal samples were collected from long-term virologically suppressed HIV-1-infected men (n=10) before (T0) and after 6 months (T6) of high concentration oral bacteriotherapy supplementation (450 × 10^9 billion bacteria, twice a day of Vivomixx®) and from age- and gender-matched healthy controls (n=5). Analysis of fecal microbiota composition was performed by 16S rRNA gene sequencing. The morphology of apical junctional complex and expression of Claudin-2, Occludin, E-cadherin and Zonulin were evaluated in gut biopsies through immunohistochemical assays.

Understanding whether the modulation of gut microbiota might promote a reconstitution of intestinal epithelial barrier in HIV-1-infected individuals was the main purpose of the present study. The effects of a specific probiotic preparation has been evaluated in restoring the intestinal barrier integrity by a physical point of view, analyzing the fecal microbiota composition and the Apical Junctional Complex (AJC) structure.

RESULTS

- HIV-1-infected individuals had a distinct fecal microbiota pattern characterized by a reduction of Bifidobacteriacae (p=0.0290) and Ruminococcaceae (p=0.0280) families compared to uninfected controls (Figure 1).
- HIV-1-infected men receiving oral bacteriotherapy had an increased bacterial biodiversity and richness restoration (Shannon Index: T0 vs. T6, p=0.0182; Simpson Index: T0 vs. T6, p=0.0281), with an abundance of Actinobacteria (T0 vs. T6, p=0.0448) and a decrease of Bacteroidetes levels (T0 vs. T6, p=0.0102).

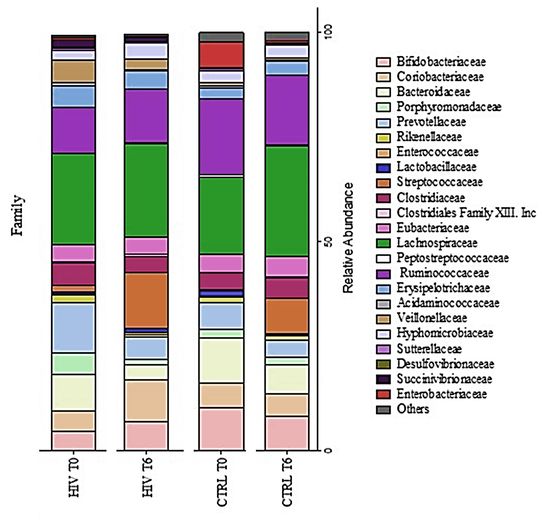

Figure 1. Microbiota compositional analysis in HIV-1-infected men and healthy individuals

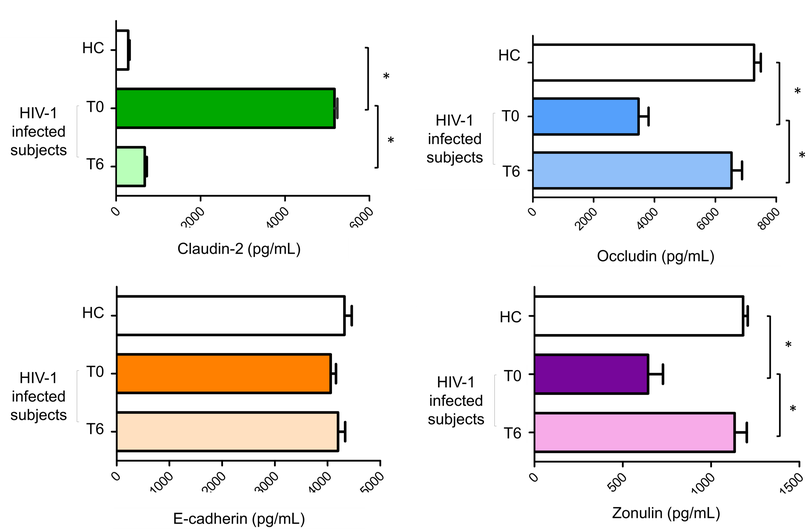

Figure 2. Oral bacteriotherapy effects on the intestinal expression of AJC proteins in HIV-1-positive patients and healthy individuals

- A restoring of intestinal apical junctional complex structure was observed (Figure 2, T0 vs T6, p<0.0001 for all analysis) after supplementation. Moreover, oral bacteriotherapy administration resulted in an increase in the levels of Occludin and Zonulin and a decrease in those of Claudin 2 in HIV-1-infected individuals (Figure 2, T0 vs T6, p<0.0001).

CONCLUSIONS

Considering the critical role of the microbiota in the HIV-1 pathogenesis, these findings suggest that six months of oral bacteriotherapy supplementation might represent a strategy to reverse the fecal microbiota alterations and reconstitute intestinal barrier integrity in ART-treated HIV-1-infected men.

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