PREVOTELLA IS RELATED TO A DYSREGULATION OF IFN AND T CELL RESPONSE IN HIV INFECTION

0228

Claudia Pinacchio[1], Giuseppe P. Innocenti[1], Letizia Santinelli[1], Eugenio Nelson Cavallari[1], Federica Frasca[1], Carolina Scagnolari[1], Guido Antonelli[1], Claudio M. Mastroianni[1], Gabriella d'Ettorre[1]

[1]Sapienza University of Rome, Rome, Italy

BACKGROUND

- Altered interplay between gut mucosa and dysbiotic microbes during HIV infection has been linked to chronic immune dysfunction, commonly characterized by high levels of IFN and immune activation markers as well as by a severe depletion of Th17 T cells in the gastrointestinal tract.

- HIV-associated dysbiosis is most commonly characterized by overall decreased diversity, with reduced abundances of the genus *Bacteroides* and increased abundances of the genus *Prevotella*.

AIM OF THE STUDY

A pilot study was performed to investigate whether a specific gut microbial communities imbalance in HIV-infected individuals could affect the antiviral defense and T cell immunity.

METHODS

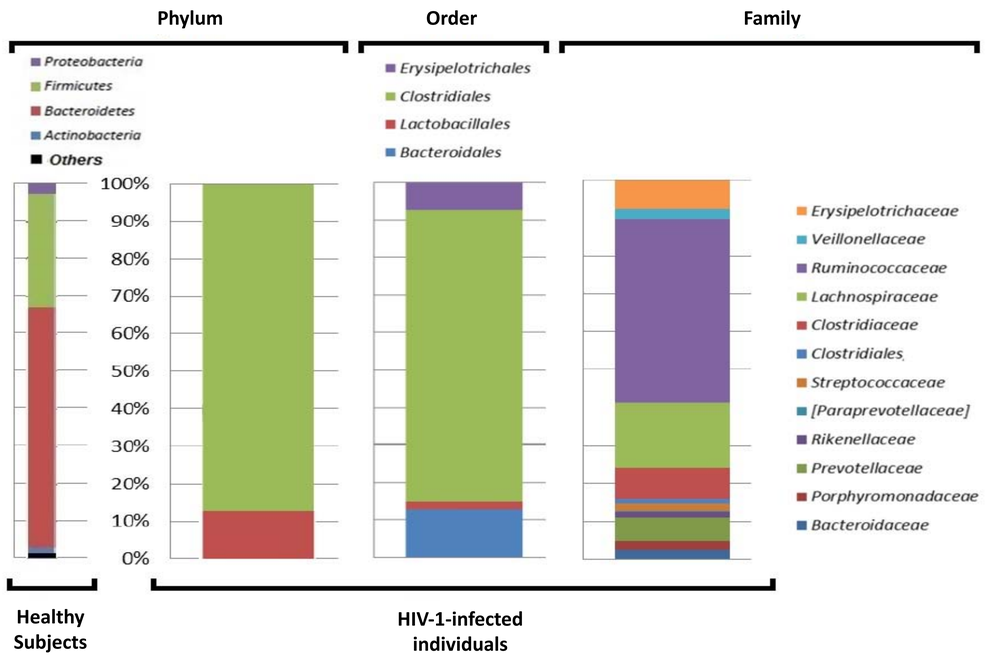
Ten HIV-infected subjects on long-term suppressive combined antiretroviral therapy (cART) underwent endoscopic procedure. Lamina propria lymphocytes were isolated from five different intestinal sites (e.g. terminal ileum, cecum, ascending, transverse, and descending colon). Phylum, Family, Class, Order and Genus identification was performed on bacterial 16S ribosomal DNA sequences obtained from fecal samples collected for all HIV-1-infected patients and five healthy controls. Measurements of CD4 and CD8 T cell activation (CD38+, HLA-DR+, CD38+HLADR+) and IL-17 expression on CD4+ (Th17) were performed by flow cytometry. Gene expression level of IFNβ, IFN receptor 1 (IFNAR1) and the well-known Interferon Stimulated Gene (ISG), Myxovirus resistance gene A (MxA), was also evaluated in gut by RT/real-time PCR. Nonparametric t-tests were used for statistical analysis.

RESULTS

Study population:

Ten successfully ART-treated HIV-1-infected Caucasian men with an average age of 46 (interquartile range [IQR]: 38,5-52,5) years old were included in this study; they have been treated for a median of 6 years (IQR: 1.75-15.75). The median of CD4+ cell count pre-cART was 255 cells/mm3 (IQR: 47.5-360) and HIV-1 RNA median value was 5.0 log/mL (IQR: 4.8-5.55). Five age- and gender-matched uninfected controls were also included in this study.

HIV-1 infection alters fecal microbiota compositional structure



Among the abundant genera of the Bacteroidetes phylum in HIV-1-infected individuals, *Prevotella* had a relative abundance of 6.10%, while *Bacteroides* of 2.53%

Association between relative abundance of *Prevotella* and IFN-related pathways, T cell immune activation and Th17 levels in HIV-1-infected patients.

Innate Immune Response to *Prevotella* genus		
IFNβ	***r*=-0.663**	***p*<0.05**
IFNAR1	***r*=-0.662**	***p*<0.05**
MxA	***r*=-0.774**	***p*<0.05**
Adaptive Immune Response to *Prevotella* genus		
CD4 HLA-DR	***r*=0.563**	***p*<0.05**
CD4 CD38	***r*=0.522**	***p*<0.05**
CD4 HLA-DR CD38	***r*=0.522**	***p*<0.05**
CD8 HLA-DR	*NA*	*NA*
CD8 CD38	***r*=0.887**	***p*<0.05**
CD8 HLA-DR CD38	***r*=0.689**	***p*<0.05**
IL-17 producing Th cells (Th17)	***r*=-0,303**	***p*<0.05**

✓ Abundance of *Prevotella* was directly correlated with CD4+38+, CD4+DR+ and CD4+38+DR+ in gut ($p<0.05$ for all these measures). Additionally, the same trend was observed for the activated CD8+ T cell subsets in the same anatomical site.

✓ By contrast, *Prevotella* levels were inversely associated with the frequencies of Th17 T cells in gut compartment.

✓ Notably, higher levels of IFNβ, MxA , and IFNAR1, were associated to lower abundance of the genus *Prevotella* in the gut mucosa.

CONCLUSIONS

Our findings suggest that abundance of the genus *Prevotella* could affect gut mucosal type I IFN pathways and modify T cell response in HIV-infected subjects.

claudia.pinacchio@uniroma1.it

ACKNOWLEDGEMENTS

The authors wish to acknowledge all the study participants who contributed to this work as well as the clinical research staff who made this research possible.