

Cannabis Use Enhances Mucosal Immunity and the Microbiome in Individuals With HIV

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INTRODUCTION

Cannabis is widely used by people living with HIV (PLWH) both recreationally and to mitigate HIV- or antiretroviral therapy (ART)-associated nausea, pain, anorexia, or other symptoms¹. Here, we evaluated immune function and intestinal health among a cohort of ART-treated, cannabis-using, and non-using PLWH. Previous work from our group has demonstrated that heavy cannabis use decreases inflammation and immune activation systemically. Thus, here we hypothesized that cannabis using PLWH would have reduced inflammation and immune activation linked with a more immunomodulatory gastrointestinal (GI) microbiome.

METHODS

Single-cell suspensions were isolated from colon biopsies from cannabis-using and non-using ART-treated PLWH. These were analyzed for cellular immune function by multiparameter flow cytometry. Plasma levels of short-chain fatty acids (SCFA) as indicators of colonic function were assessed by gas chromatography-mass spectrometry (GC-MS). GI microbial communities were profiled through 16s rRNA sequencing in the colonic mucosa. Cannabis use or non-use was verified in all participants by liquid chromatography-mass spectrometry (LC-MS).

Table 1: Demographic and clinical data of the participants in this study

Variable	Group		Total
	Cannabis-users	Non-users	
No. of volunteers	26	19	45
Age (Mean± SD)	43.1 ± 13.17	49.9 ± 9.19	46 ± 12.03
Gender (n, (%))			
Male	20 (76.9)	17 (89.5)	37 (82.2)
Female	6 (23.1)	2 (10.5)	8 (17.8)
HIV infected (n,(%))			
Yes	14 (53.8)	13 (68.4)	27 (60)
No	12 (46.2)	6 (31.6)	18 (40)

Cannabis use does not alter gut T cell frequencies

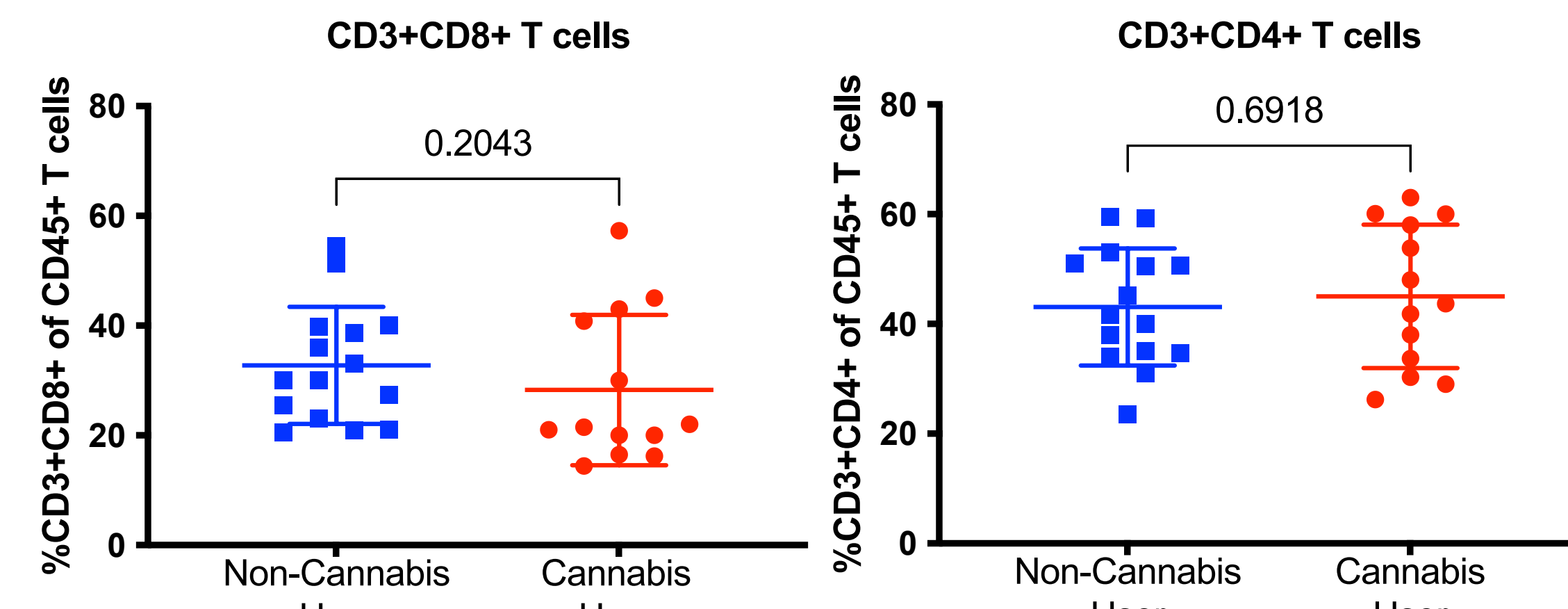


Figure 1. No difference in CD4+ and CD8+ T cell frequencies in cannabis users compared to non-users. A single point represents each individual. Horizontal bars indicate the median value. Significance was calculated by the Mann-Whitney test, and $p < 0.05$ was considered significant.

Cannabis use decreases T-cell activation and increases cell death

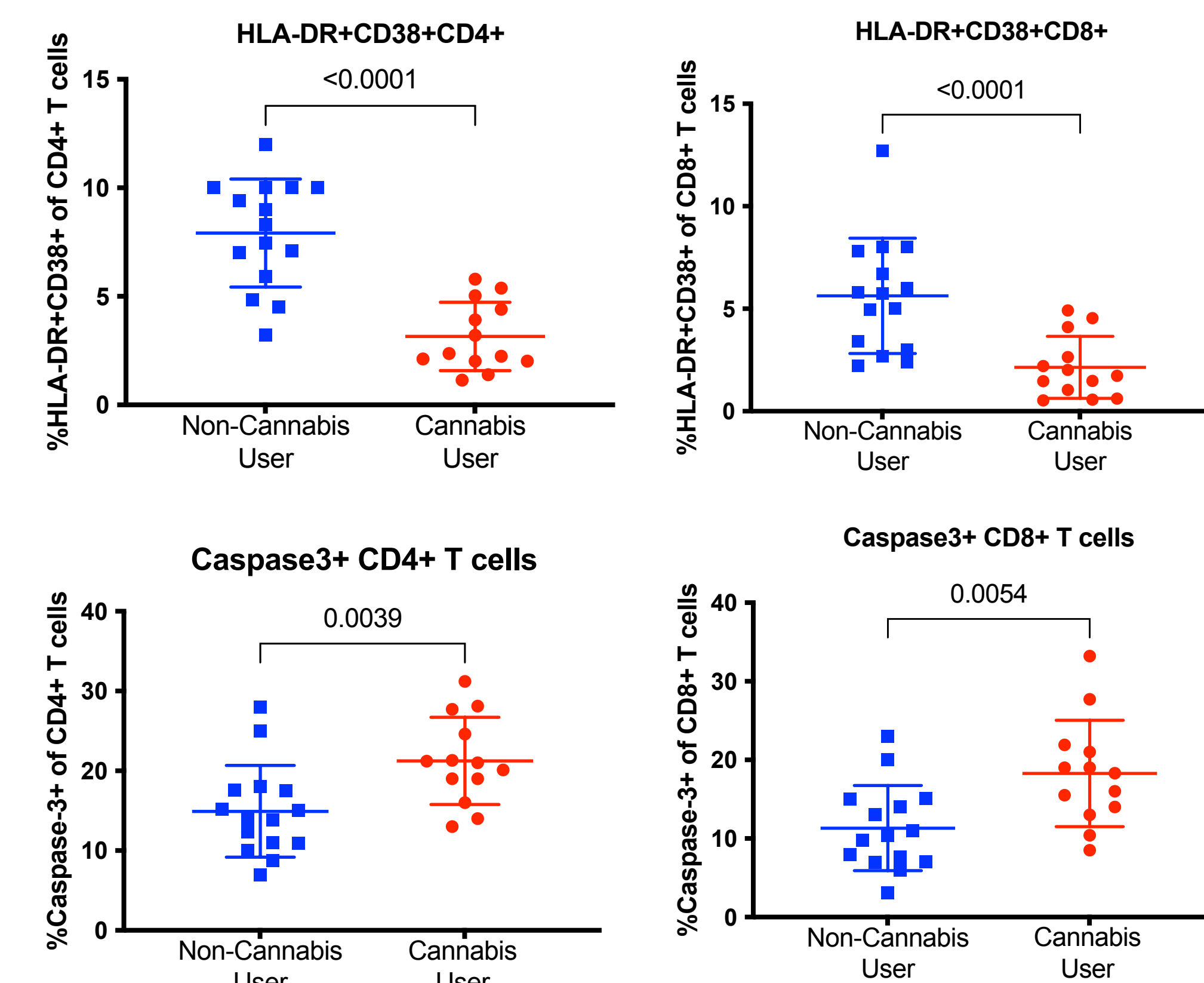


Figure 2. The frequency of activated T-cells was significantly lower in cannabis users compared to non-users as measured by HLA-DR+CD38+ T cells. A single point represents each individual. Horizontal bars indicate the median value. Significance was calculated by the Mann-Whitney test, and $p < 0.05$ was considered significant.

People living with HIV have significantly less short-chain fatty acid production

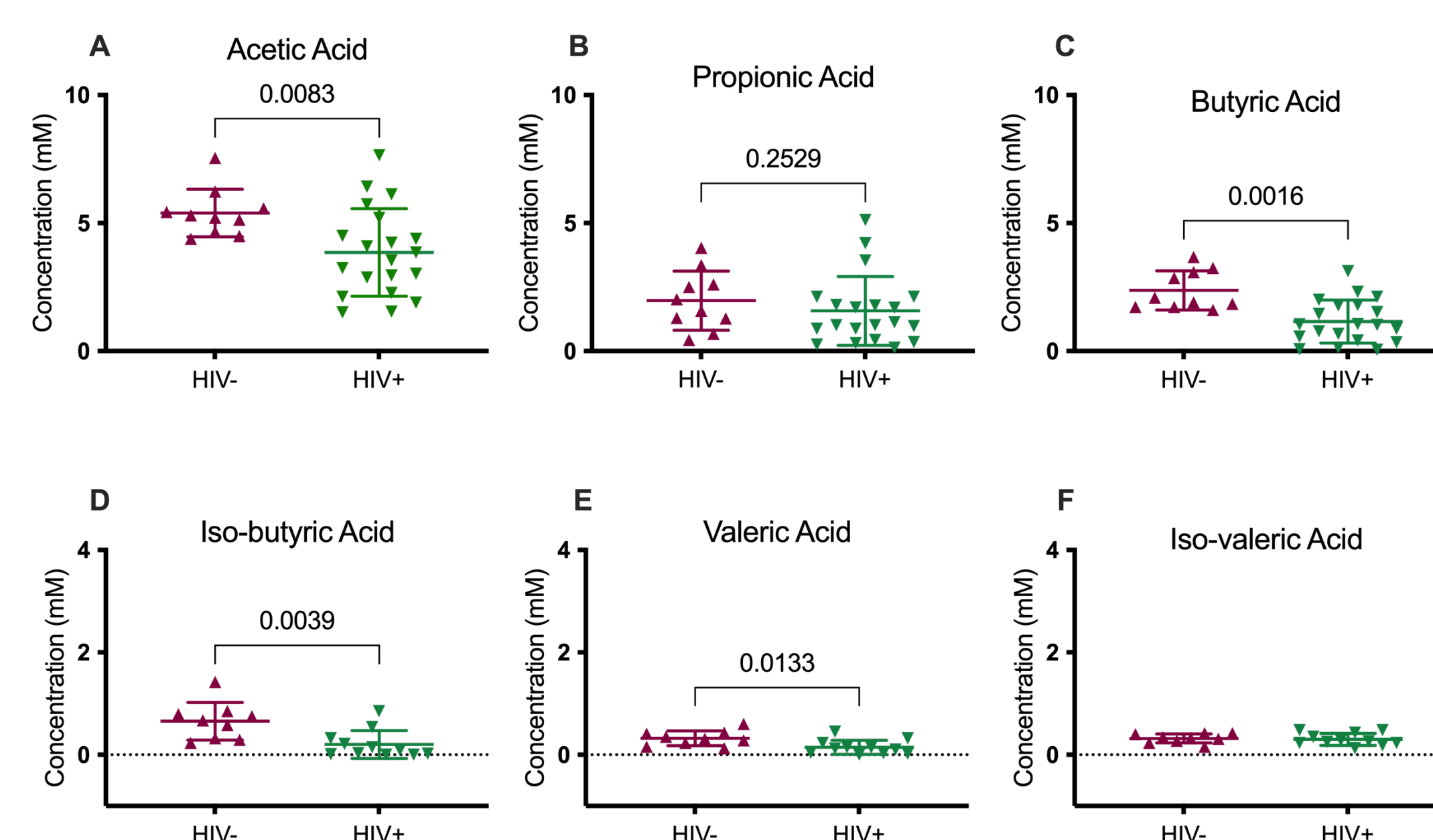


Figure 3. Levels of beneficial short-chain fatty acids decreased in people living with HIV. A single point represents each individual. Horizontal bars indicate the median value. Significance was calculated by the Mann-Whitney test, and $p < 0.05$ was considered significant.

Cannabis use alters the functionality of B cells and decreases the production of pro-inflammatory cytokines from B cells

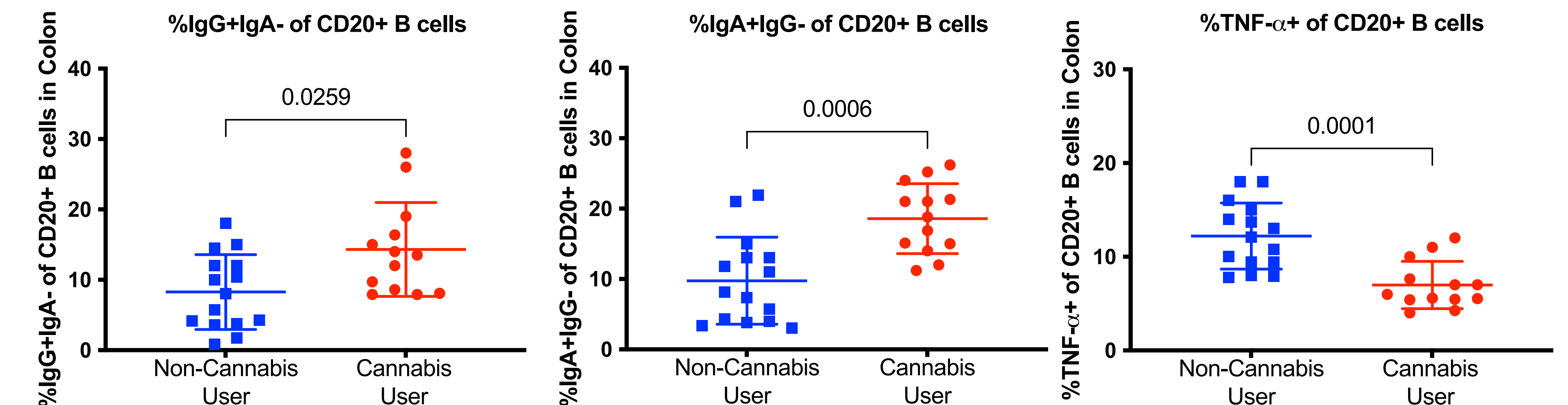


Figure 4. Cannabis use increases the frequency of IgG+ and IgA+-producing B cells and reduces the production of inflammatory cytokines. A single point represents each individual. Horizontal bars indicate the median value. Significance was calculated by the Mann-Whitney test, and $p < 0.05$ was considered significant.

Cannabis alters the gut microbiome in people living with HIV and may increase the abundance of beneficial bacteria

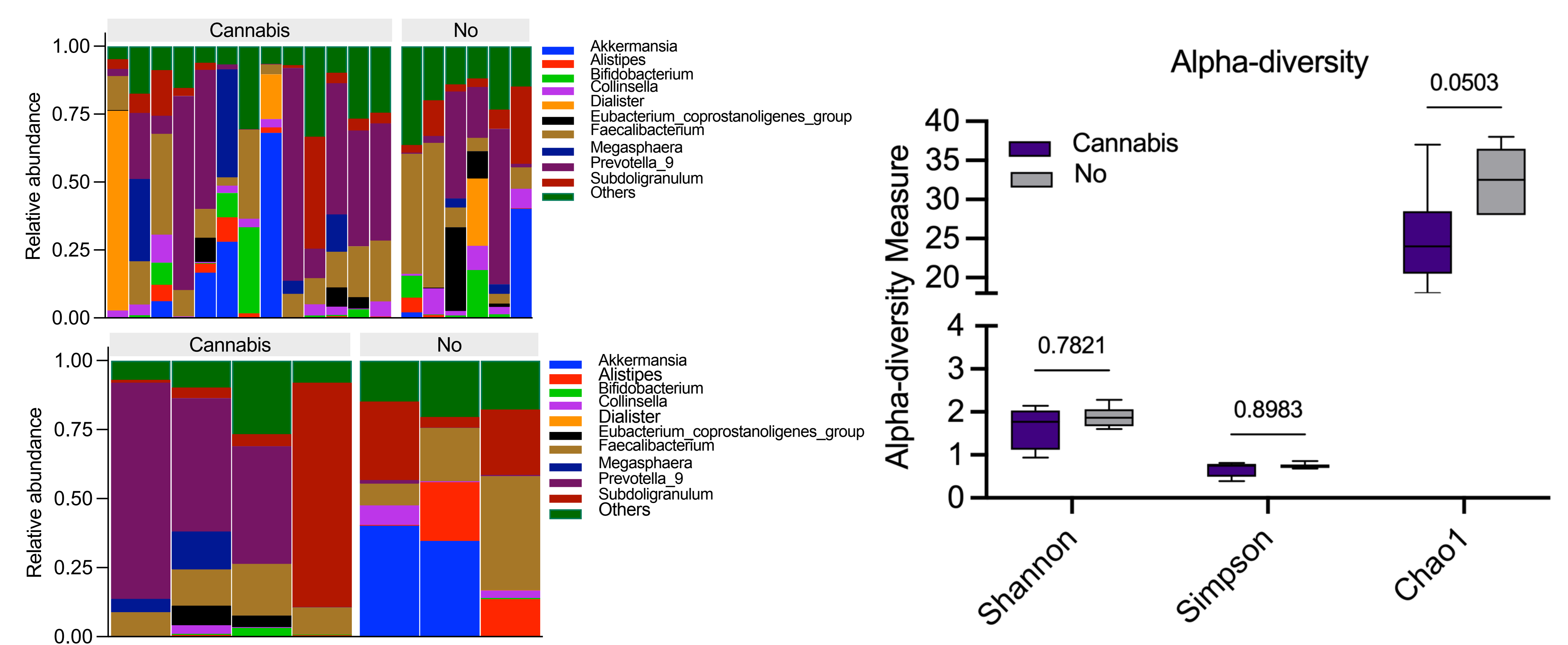


Figure 5. Microbial alpha-diversity analyses and microbial abundance profiling in stool samples among cannabis users and non-users. Taxonomic composition at the genus level. There were no statistically significant differences in alpha-diversity indices, including Shannon's index ($p = 0.7821$), Simpson's index ($p = 0.8983$), and Chao1's index ($p = 0.0503$) among cannabis users and non-users.

Cannabis use increases short-chain fatty acid production

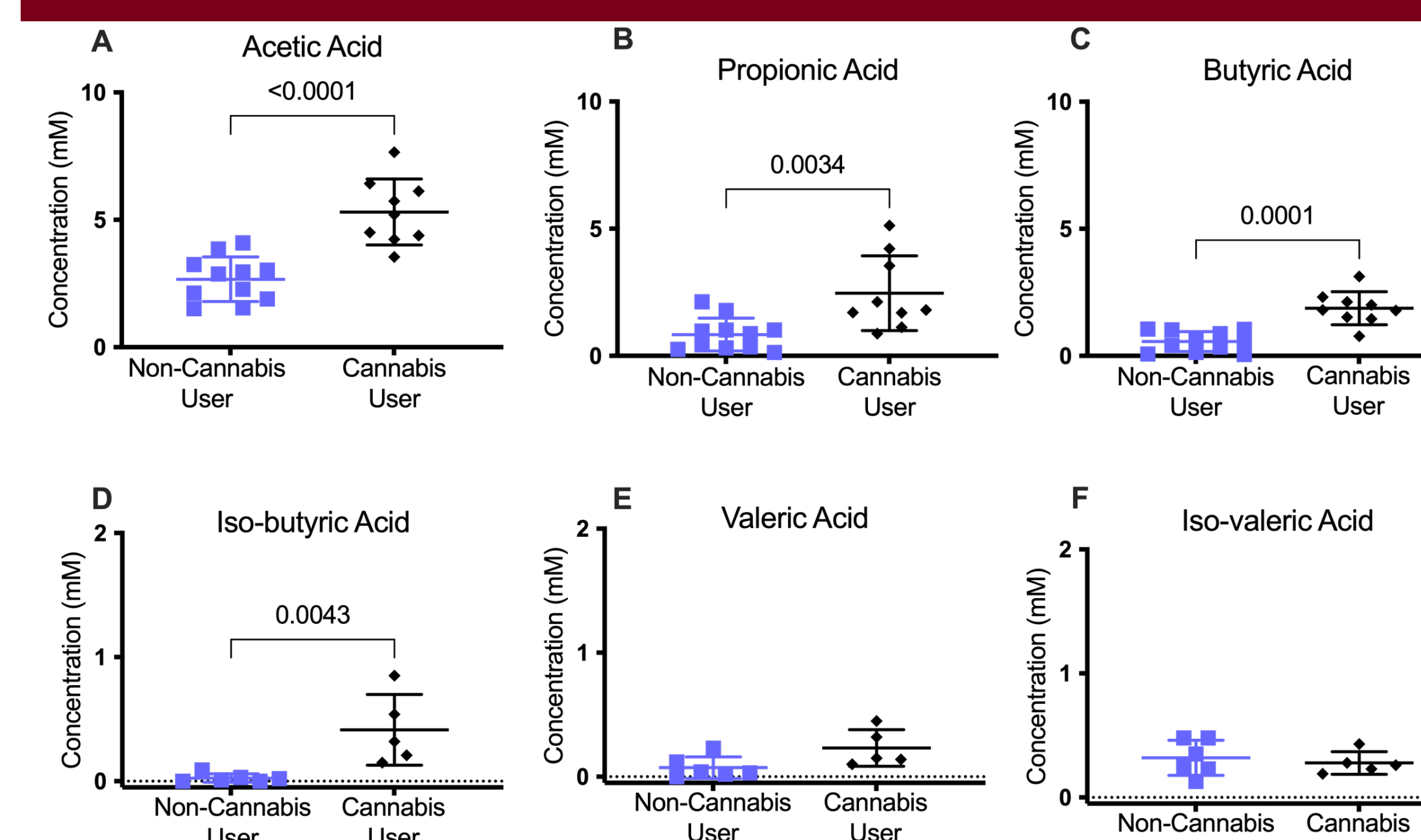


Figure 6. Levels of beneficial short-chain fatty acids increased in cannabis users compared to non-users. A single point represents each individual. Horizontal bars indicate the median value. Significance was calculated by the Mann-Whitney test, and $p < 0.05$ was considered significant.

CONCLUSION

ART-treated cannabis using PLWH had significantly lower frequencies of activated CD4+ and CD8+ T-cells and TNF- α +CD20+B cells in the colon, suggesting lower inflammation and immune activation as compared to non-cannabis users in mucosal tissues. Cannabis use has the potential to alleviate HIV-associated inflammation through alterations in microbial community structure and function. Overall, this study provides important insights into the impact of cannabis use on immunity and the microbiome of PLWH and its impacts on GI health.

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REFERENCE

1. J. A. Manuzak *et al.*, Heavy Cannabis Use Associated With Reduction in Activated and Inflammatory Immune Cell Frequencies in Antiretroviral Therapy–Treated Human Immunodeficiency Virus–Infected Individuals. *Clinical Infectious Diseases* **66**, 1872–1882 (2018).