RELEVANCE OF CMV AND EBV CO-INFECTION TO CHRONIC INFLAMMATION IN HIV ELITE CONTROLLERS

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Introduction

Elite controllers (EC) present with chronic inflammation and remain at increased risk of developing non-AIDS comorbidities. Microbial translocation is a contributor to chronic inflammation and CMV co-infection has been recently linked to increased microbial translocation. We previously reported that CMV seropositivity was associated with elevated epithelial gut damage and microbial translocation in ART-treated PLWH and HIV-uninfected controls. As Canada has one of the lowest CMV co-infection prevalence in the world, we evaluated the link between CMV seropositivity, microbial translocation, and inflammation among EC.

Methods

Study samples were collected from 37 EC (25 CMV+, 12 CMV-). By HLA typing, we categorized participants with/without protective HLA alleles (B*27, B*57, n=16). We measured CD4 and CD8 T-cell counts, anti-CMV IgG and anti-EBV IgG titers, markers of epithelial gut damage REG3α and I-FABP, markers of microbial translocation LPS, sCD14 and B-D-Glucan (BDG), as well as total IgG, IgM, IgA, IL-1β, IL-6 and kynurenine/tryptophan.

Population Characteristics

Table 1, Participant Characteristics

	Elite controllers (n=35)
Age in years	
Median (IDR) Range	45 (39-50) 26-72
Sex	
Male, n (%) Female, n (%)	21 (60.0) 14 (40.0)
CD4 T-cells/µL	
Median (IQR) Range	650 (552-823) 290-1090
CD8 T-cells/µL	
Median (IQR) Range	690 (409-968) 180-1460
CD4/CD8	
Median (IQR) Range	1.1 (0.8-1.4) 0.3-2.5
HIV VL (log_{10}copies/mL)	
Median (IQR) Range	<1.7 NA
Years on ART	
Median (IQR) Range	NA NA
CMV status	
Positive (%)	25 (71.4)
Anti-CMV IgG (IU/mL)	
Median (IQR)	23.9 (14.6-28.6)
Anti-EBV IgG (IU/mL)	
Median (IQR)	17.1 (8.3-22.1)

Results

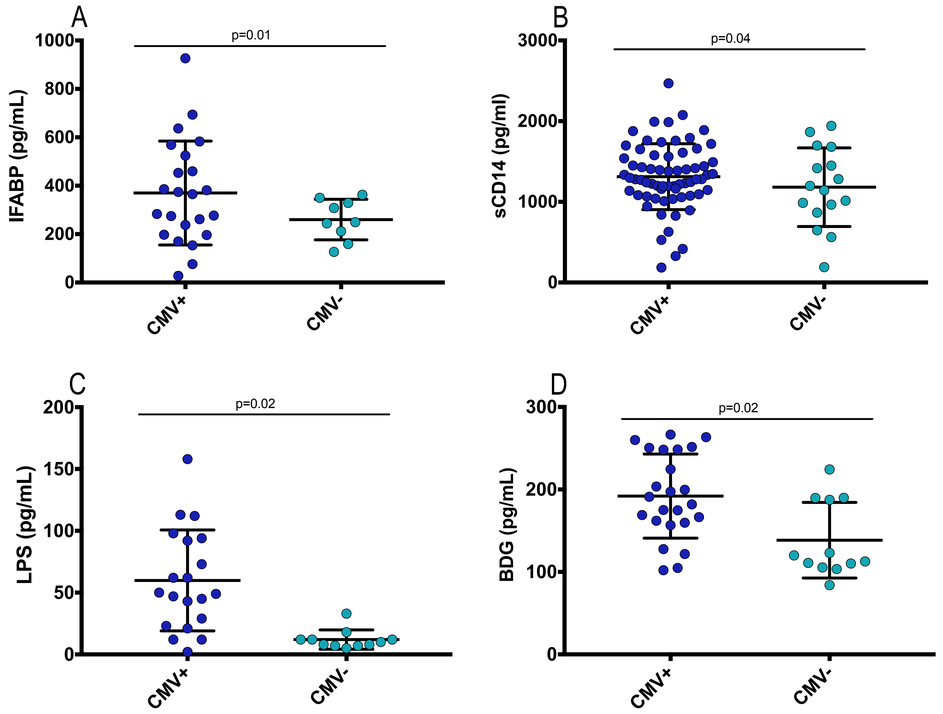

Figure 1. Plasma levels of markers of epithelial gut damage and microbial translocation in HIV elite controllers. CMV-seropositive elite controllers have elevated plasma levels of (A) I-FABP, (B) sCD14, (C) LPS, and (D) BDG compared to their CMV-seronegative counterparts.

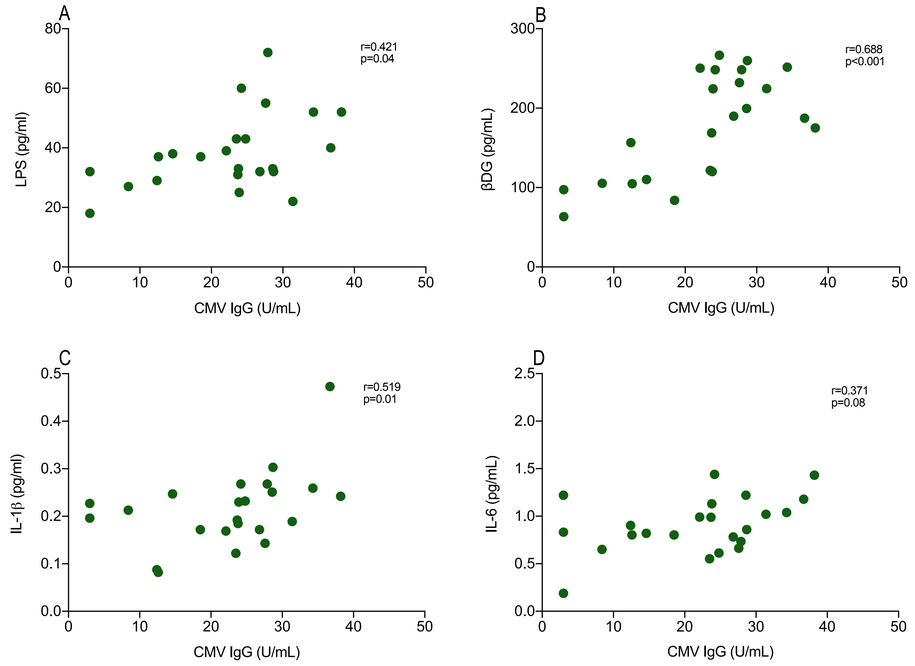

Figure 2. Correlations between anti-CMV IgG titers and plasma levels of (A) LPS, (B) BDG, (C) IL-1B, and (D) IL-6 in CMV seropositive EC.

Results Cont.

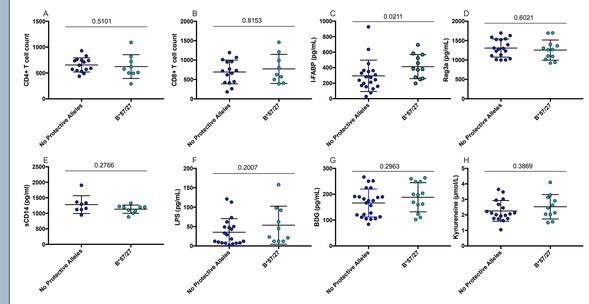

Figure 3. Comparison of (A) CD4+ T cell count, (B) CD8+ T cell count, (C) Intestinal Fatty Acid Binding Protein (I-FABP), (D) Reg3a, (E) sCD14, (F) LPS, (G) (1→3)-B-D-Glucan, and (H) Kynureneine amongst elite controllers with and without HLA-protective alleles.

Conclusions

Markers of epithelial gut damage, microbial translocation, and inflammation were higher in CMV seropositive EC, irrespective of protective HLA alleles. Therefore, CMV co-infection emerges as an important contributor to gut damage and microbial translocation and may contribute to non-AIDS comorbidities in EC.

Citations

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