INTRODUCTION

Interleukin-32 (IL-32) is a multi-isoformal cytokine (IL-32α, IL-32β, IL-32γ, IL-32bb, IL-32bc and IL-32bd) that has received growing attention as an important component in numerous autoimmune and inflammatory disorders. Recent reports have highlighted the therapeutic potential of IL-32 regulation during viral infections. Few studies have investigated the expression of IL-32 in chronic HIV infection. This study aimed to characterize both the anti-viral properties of IL-32 and the cytokine’s relationship with the IFN system in chronically HIV infected patients.

PATIENTS AND METHODS

Patients

Peripheral blood samples from 83 HIV-positive patients of both genders, ranging in age from 18 to 65 years, were collected at the Pasteur Institute’s Hospitals. All patients had been infected with the HIV-1 subtype B strain and were naive for antiretroviral treatment. No patient had any concurrent acute illness or infection including CMV disease, mycobacterium tuberculosis, hepatitis B or C and or herpes infections.

Blood samples were separated from whole blood by centrifugation using Ficoll/Hypaque (Sigma, St Louis, MO, USA), according to the manufacturer’s protocol, and was retro-transcribed as previously specified. The housekeeping gene β-2 microglobulin was used as an internal control. Gene expression values were calculated by employing the comparative threshold cycle (Ct) method.

Evaluation of the relationship between IL-32 mRNA levels and clinical parameters

Our results also indicated the existence of weak correlations between transcript levels of IL-32α and those of MxA (r=0.45; p=0.01), MX1 (r=0.39; p=0.03) and APOBEC3F (r=0.35; p=0.01) measured in PMBC collected from HIV-infected patients (Fig. 5, Panel A, C and E). Differently the transcript levels of IL-32α were more strongly correlated to the gene expression of MxA (r=0.70; p<0.001) and APOBEC3F (r=0.69; p<0.001) (Fig. 5, Panel B and D). The modulation of IL-32α gene expression levels and CD4+ T cells in HIV+ patients expressing higher mRNA levels (IL-32α: r=0.7; p<0.001) was determined after IFNα treatment (Fig. 4 Panel A and B, MXA: r=0.70; p<0.001, APOBEC3G: r=0.72; p<0.001, APOBEC3F: r=0.73; p<0.001). The IL-32α expression was positively correlated to the number of CD8+ T cells (r=0.72; p<0.001). The IL-32α expression was positively correlated to the number of CD8+ T cells (r=0.72; p<0.001). We failed to detect any significant association between IL-32α and the gene expression levels and CD4 T cell count in our studied group (IL-32α: r=0.35; p<0.07; IL-32β: r=0.17; p=0.57). In conclusion, this study provides novel evidence that IL-32α participates in the antiviral immune responses in HIV-infected patients. The modulation of IL-32 isoforms on type I and III IFNs might merit further investigation to better understand the host immune response in HIV-infected patients.

RESULTS AND CONCLUSIONS

In vivo and in vitro relationship between IL-32 and the type I IFN pathway

To better characterize the antiviral properties of IL-32 and the cytokine’s relationship with the IFN system, we first examined ex vivo the ability of IL-32 to regulate the expression of some ISGs in IL-32α or IFNα-stimulated PBMC. ISGs were assessed by quantitative RT-PCR. To better characterize the antiviral properties of IL-32 and the cytokine’s relationship with the IFN system, we first examined ex vivo the ability of IL-32 to regulate the expression of some ISGs in IL-32α or IFNα-stimulated PBMC. ISGs were assessed by quantitative RT-PCR. To better characterize the antiviral properties of IL-32 and the cytokine’s relationship with the IFN system, we first examined ex vivo the ability of IL-32 to regulate the expression of some ISGs in IL-32α or IFNα-stimulated PBMC. ISGs were assessed by quantitative RT-PCR. To better characterize the antiviral properties of IL-32 and the cytokine’s relationship with the IFN system, we first examined ex vivo the ability of IL-32 to regulate the expression of some ISGs in IL-32α or IFNα-stimulated PBMC. ISGs were assessed by quantitative RT-PCR. To better characterize the antiviral properties of IL-32 and the cytokine’s relationship with the IFN system, we first examined ex vivo the ability of IL-32 to regulate the expression of some ISGs in IL-32α or IFNα-stimulated PBMC.

The modulation of IL-32α gene expression levels and CD4+ T cells in HIV+ patients expressing higher mRNA levels (IL-32α: r=0.7; p<0.001) was determined after IFNα treatment (Fig. 4 Panel A and B, MXA: r=0.70; p<0.001, APOBEC3G: r=0.72; p<0.001, APOBEC3F: r=0.73; p<0.001). The IL-32α expression was positively correlated to the number of CD8+ T cells (r=0.72; p<0.001). We failed to detect any significant association between IL-32α and the gene expression levels and CD4 T cell count in our studied group (IL-32α: r=0.35; p<0.07; IL-32β: r=0.17; p=0.57). In conclusion, this study provides novel evidence that IL-32α participates in the antiviral immune responses in HIV-infected patients. The modulation of IL-32 isoforms on type I and III IFNs might merit further investigation to better understand the host immune response in HIV-infected patients.