INTRODUCTION

There are several host factors that can affect the susceptibility to HIV and progression of the disease in an infected individual. These include natural defenses that act at different points in the viral life cycle by the APOBEC and TRIM family genes, A32 deletion in theCCR5 genes and SNPs in different genes encoding the chemokine receptors.

Recently polymorphism on the IFNγ3 gene (IL-28B) has been shown to have an impact on the on IL-28B cytokine secretion and thereby its antiviral activity against several viruses as shown in figure 1.

Figure 1: IFNγ3– Signaling pathway (Donnelly et al. 2011)
The wild type genotypes CC at rs12979860 and TT at rs8099917 have been shown to be associated with better treatment response of HIV infection.

MATERIALS AND METHODS

• This study was conducted between August 2013 and September 2015 after approval from Institutional Review Board.

• Flow cytometry (BD FACSCount™, Beeton Dickinson, USA) for estimation of Absolute CD4+ cells and CD4+CD8− T-cell counts and average CD3 T-cell counts and CD4CD8 T-cell ratio.

• IL-28B Polymorphism detection – PCR-RFLP using Restriction Enzymes BstUI and RevUI (New England BioLabs, UK) for rs12979860 and rs8099917 and analyzed by gel electrophoresis as shown in figure 2.

• To analyze the association of IL-28B polymorphism with CD4+CD8− T-cell counts, IL-2B plasma level, IL-28 mRNA expression in HIV infected individuals after 6-9 months of ART.

• To analyze the association of IL-28B polymorphism with CD4+ cells, CD4+CD8− T-cell counts, IL-28B plasma level, IL-28 mRNA expression with HIV viral load in treatment naïve HIV infected individuals.

• To analyze the association of IL-28B polymorphism with viral load and IL-28 mRNA expression in HIV infected individuals undergoing HAART.

• To analyze the association of IL-28B polymorphism with IL-28 mRNA expression and IFN-α2a response in HIV infected individuals.

• To analyze the association of IL-28B polymorphism with CRT, CD3+ and CD4+CD3− in HIV infected individuals.

• To analyze the association of IL-28B polymorphism with CD4+CD8− T-cell ratio in HIV infected individuals.

• To analyze the association of IL-28B polymorphism with CD4+CD8− T-cell counts in HIV infected individuals.

• The IL-28 mRNA expression was calculated using Gen5 software.

• The IL-28mRNA expression was quantified by Real Time PCR. The total cellular RNA was extracted using QIAamp® RNA Easy Minikit from PBMCs.

• HIV-1 viral load was quantified by Real Time PCR using the total RNA extracted from plasma in Abbott m200® automated system.

• There was a significant increase (p=0.0001) in the median CD4+ T-cell count, CD4+CD8− and reversal of CD4CD8 ratio following 6-9 months of ART in HIV infected individuals.

• There was a significant association of CC genotype at rs12979860 (p = 0.03) with higher CD4+ T-cell count among treatment naïve HIV infected individuals.

• There was a significant (p = 0.63) association of CC genotype with increase in CD4CD3− following 6-9 months of ART when compared with CT and TT.

• There is no correlation (p>0.05) of IL-28B polymorphism with neither IL-28B plasma level nor IL-28B mRNA expression among treatment naïve HIV infected individuals and controls.

• The median IL-28 mRNA expression was significantly (p = 0.001) higher in healthy controls when compared to HIV-1 infected individuals (before and after ART).

• There was a significant (p = 0.007) correlation between HIV-1 viral load and IL-28B mRNA expression in HIV infected individuals.

• There was no association between IL-28 plasma level (IL-2c mRNA and CD4+, CD8+ and CD4% and CD3% and in HIV infected individuals before and after ART).

• There was no significant difference (p = 0.05) in the IL-28B plasma level in HIV-1 infected individuals and healthy controls.

CONCLUSIONS

Though in vitro studies have shown anti-HIV activity of IL-28 by inhibiting HIV replication, in vivo functional studies with larger sample size are warranted to understand the IFN-α mediated control of HIV replication in HIV infected individuals.

REFERENCES


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A PILOT STUDY TO LOOK AT THE EFFECT OF IL-28B POLYMORPHISM ON IL-28B EXPRESSION AND IMMUNOLOGICAL RECOVERY AMONG HIV INFECTED INDIVIDUALS

FOLLOWING ANTIRETROVIRAL THERAPY

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Figure 2: A representative picture of PCR-RFLP gel electrophoresis.

Figure 3: Frequencies of IL-28B genotypes in cases and controls.

There was a significant association of CC genotype at rs12979860 with CD4+, CD4CD8− and reversal of CD4CD8 ratio following 6-9 months of ART in HIV infected individuals.

The difference in the median of IL-28mRNA expression between HIV infected individuals and controls as shown in figure 5b.

Figure 5: (A) Association of IL-28 mRNA expression with HIV viral load in HIV infected individuals.

(b) Difference in IL-28mRNA between cases and controls

Figure 4: Correlation of Absolute CD4+ T-cell and CD4CD8− with the genotypes.

Figure 6: Flowcytometry shows the expression of CD4, CD8 and total lymphocytes among individuals with different genotypes.