P0035
Paper Poster Session
HIV biomarkers, resistance and diagnostics

Analysis of the mRNA expression of DNA damage response genes in HIV-1 infected patients

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Background: Though combined antiretroviral therapy (cART) in HIV-1 positive patients allows a massive suppression of viral replication, many aspects of persistance and pathogenesis of infection are still unknown.
It has been reported that virus-induced cell killing is triggered by viral integration. Infection by wild-type HIV-1, but not an integrase-deficient mutant, induced the death of activated primary CD4 lymphocytes. Similarly, integrase inhibitors abolished HIV-1-induced cell killing both in cell culture and in $CD4^+$ T cells from acutely infected subjects. The mechanism of killing during viral integration involved the activation of DNA-dependent protein kinase (DNA-PK), a central integrator of the DNA damage response, which caused phosphorylation of p53 and histone H2AX.
The aim of the study was to evaluate if Inhibitor Integrase (INI) containing regimen could affect mRNA expression profile *of* DNA damage response genes involved, in HIV infected patients.
Material/methods: Thirty-two PBMC samples from HIV+ patients (14 treatment naïve and 18 treated with ART containing INI) and 10 sample from healthy donors (HD) were collected; mRNA levels of FasR, XRCC1, Lig IIIα, Parp-1, DNA PkI, DNA PkII were evaluate using Syber Green Real time PCR (Agilent Technologies). All HIV treated patients had undetectable viremia. Results *were* normalized using housekeeping genes beta-actin (ΔCT*)*. The fold-difference of expression levels between three groups were measured comparing Δ*CT* values. Differences between the groups were analyzed for statistical significance using T-test.
Results: A significantly higher expression of mRNA levels of XRCC1 and DNA PkI was detected in HIV infected individuals than in HD (XRCC1: ΔCT naïve =15.9; ΔCT INI-cART=16.3 and ΔCT HD= -5.5; $p<0.05$. DNA Pk1: ΔCT naïve =17.1; ΔCT INI-cART=14.2 and ΔCT HD=-2.2; $p<0.05$). The levels of FasR were higher in naïve patients than in INI-cART patients and HD, but the difference did not reach statistically significant values (ΔCT naïve =8.6; ΔCT INI-cART=4.6 and ΔCT HD=-0.4). mRNA expression of Parp-1 was lower in naïve patients than INIs-cART group, who showed levels of mRNA for parp-1 similar to HD (Parp-1: ΔCT naïve= 1,6; ΔCT INI-cART= 6.5; ΔCT HD 8.1; $p>0.05$). No significant differences in the expression of DNA Pk II and Lig IIIα mRNA levels were detected
Conclusions: The expression levels of some DNA damage genes are higher in HIV+ patients than in healthy donors. Interestingly, no significant difference between naïve and INI-cART treated patients was observed. This data suggests that a cellular damage persist despite suppression of viral replication.