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The frequency of HIV-specific CD8 T lymphocytes is inversely correlated to HIV DNA levels in untreated infected children

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Background

HIV infection during the perinatal period differs from infection during adulthood by clinical progression, dynamic of viral replication, level of thymic activity and maturity of the immune system at time of infection.

HIV-DNA level in PBMC has recently been shown to be an independent predictor of disease progression. In PBMC, HIV-DNA is present as provirus and as well as non-integrated DNA in recently infected cells.

Most studies report the absence of association between the frequency of HIV-specific IFN- γ producing CD8 T lymphocytes and plasma viral load. However, CD8 T lymphocytes recognize cell-associated viral peptides but not free virions. Therefore, we investigated whether any association could be found between HIV-DNA load in PBMC and the HIV-specific CD8 T lymphocytes frequency.

Method

A cross-sectional analysis of immune and viral parameters was performed on 44 HIV-infected children (median 7.8 yrs, 0.08-18.6) that were untreated at time of biological assessment. Frequency of IFN-γ producing CD8 lymphocytes in response to Env-Gag-Pol antigens was determined using the ELISPOT technique. HIV-RNA level was determined by PCR (monitor 1.5, Roche). HIV DNA level

was determined in total PBMC, using real time PCR in LTR (ANRS method). Associations between quantitative variables were defined by Pearson's partial correlations. Partial correlation measures the strength of relationship between two variables, controlling for the effect of one or more other variables.

Results

HIV-DNA level in PBMC was directly correlated with HIV-RNA level in plasma (r=0.454, p<0.003), inversely correlated to CD4 % (r=0.328, p<0.04) and was independent of age. The frequency of HIV-specific CD8 lymphocytes was directly correlated to age (r=0.402, p<0.02), indirectly correlated to HIV-DNA (r=-0.338, p<0.04) independently of plasma HIV-RNA, CD4 and CD8 levels. No correlation was observed between HIV-specific CD8 T lymphocytes and HIV-RNA, CD4% or CD8%.

Conclusion

In untreated HIV-infected children, the intensity of the HIV-specific CD8 response increases with age. The negative association between the frequency of the HIV-specific CD8 T lymphocytes and HIV DNA levels in PBMC supports an antiviral role of these immune effectors.