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CD4+ and CD8+ T Cell Activation are Strongly Associated with HIV-1 DNA in Resting CD4+ T Cells

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Background

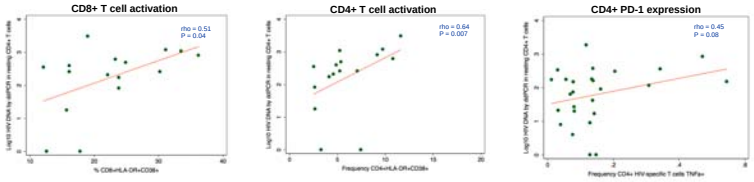
- The association between the host immune environment and the size of the HIV reservoir has not been well defined.
- There are multiple assays used to measure the HIV reservoir and it is not clear which assay(s) should be used for eradication studies.
- A comparative analysis of multiple different approaches of measuring the reservoir was recently performed (Eriksson et al, PLoS Path 2013).
- Here, we explored the association between HIV persistence as defined by these assays and the level of T cell activation and function.

Methods

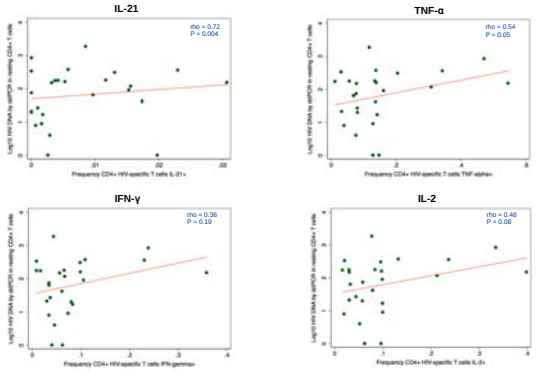
- Thirty patients were studied: 10 who started therapy during acute/ early infection and 20 who initiated treatment during chronic infection. All subjects were on suppressive ART for ≥ 36 months and had >350 CD4+ T cells/ul.
- Multiple different assays to measure viral persistence were performed simultaneously: viral outgrowth assay, droplet digital PCR (ddPCR) for HIV-1 DNA and 2-LTR circles in PBMCs and resting CD4+ T cells, *Alu* PCR for integrated HIV-1 in PBMCs and resting CD4+ T cells, and a single copy assay for plasma virus.
- HIV DNA and RNA was also measured in rectal biopsy cells using qPCR in 19 of the subjects.
- Flow cytometry was performed to measure frequencies of activated and HIV-specific T cells in blood.
- Spearman rank correlation coefficients were calculated.

Results

The frequency of CD4+ and CD8+ T cells expressing activation markers are directly associated with the frequency of resting cells harboring HIV DNA



HIV-specific CD4+ T cells are positively correlated with total HIV DNA in resting cells by ddPCR



Results

- No consistent associations were noted between activation markers or HIV specific T cells and levels of RNA or DNA in rectal cells.
- Non-significant negative associations were observed between HIV-specific CD4+ T cells and the frequency of latently infected cells by the viral outgrowth assay.

Conclusions / Implications

- The frequency of CD4+ and CD8+ T cells expressing activation markers was strongly associated with the frequency of resting cells harboring HIV DNA.
- The frequency of HIV-specific CD4+ cells was also associated with the frequency of resting cells harboring HIV DNA.
- It is unclear whether T cell activation is a cause or consequence of HIV persistence.
- However, if T cell activation was to drive persistence, this may have implications for reactivation strategies, as reversal of latency, in the absence of effective killing and complete suppression of viral replication, could lead to an increase in reservoir size.
- Further studies are needed to better define the relationship between T cell activation and reservoir size.

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