



484-M: INCREASED T CELL TURNOVER WITH HIV INFECTION CORRELATES STRONGLY WITH IMMUNE ACTIVATION AND DOES NOT NORMALIZE AFTER 52 WEEKS OF HAART

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Previous observations

- CD4+ lymphopenia is a cardinal manifestation of HIV infection, but the precise mechanisms of this depletion are unknown.
- With HAART, CD4 counts recover although often incompletely despite viral suppression to <50 copies/ml.
- HIV infection leads to a state of immune system activation with increased T cell turnover.
- The role of this increased T cell activation and turnover in CD4 depletion with HIV infection and in CD4 recovery with HAART is unknown.

Purpose of the study

- To examine the impact of T cell activation and T cell turnover on CD4 lymphopenia in HIV infection and on CD4 lymphocyte recovery following initiation of HAART.

Methods

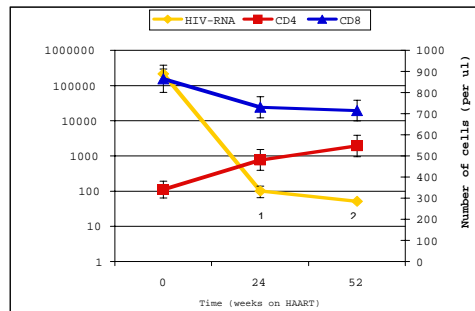
- Immunophenotypic analysis of cryopreserved PBMCs from 32 ARV-naïve HIV+ patients collected at weeks 0 and 52 of HAART using:
- markers of activation (HLA-DR and CD38)
 - markers of recent proliferation/turnover (intracellular Ki67)

Baseline patient characteristics:

	Mean	Range
Age	38	25 – 49
HIV-RNA (copies/ml)	5.3 log	3.4 – 6.4 log
CD4 count (cells/ul)	341	6 – 924
% CD4	19	1 – 39
CD8 count (cells/ul)	865	34 – 1823
% CD8	55	16 – 74
CD4:CD8	0.4	0.02 – 1.2

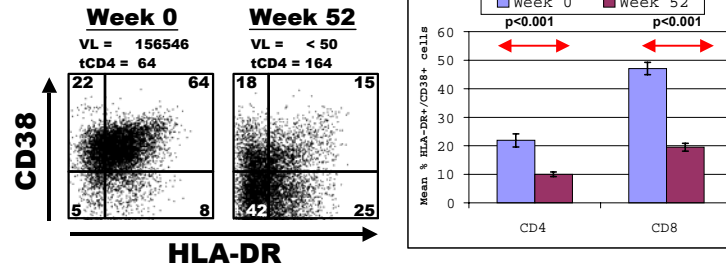
Results

1- Immunological and virological changes of study patients after initiation of HAART



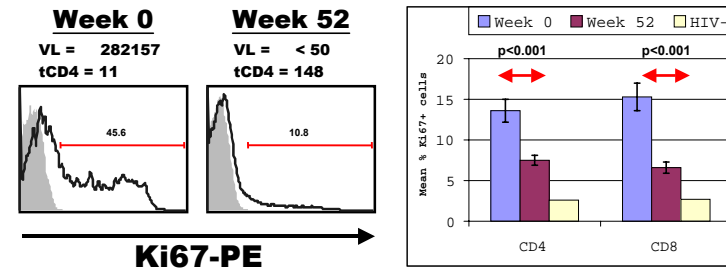
¹ Viral load <50 copies/ml in all but 7 patients
² Viral load <50 copies/ml in all but 2 patients

2- Increased activation of CD4+ and CD8+ T cells in HIV-infected patients declines after 52 weeks of HAART.



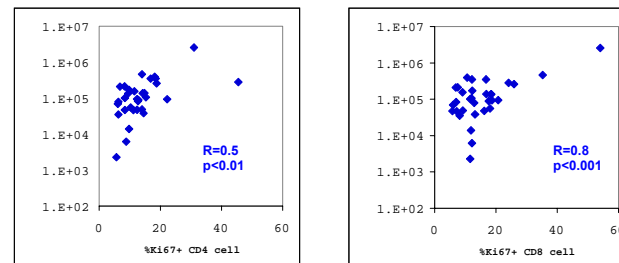
Example of dot plot of HLA-DR and CD38 expression in CD4+ T cells

3- Increased turnover of CD4+ and CD8+ T cells in HIV-infected patients declines but does not normalize after 52 weeks of HAART.

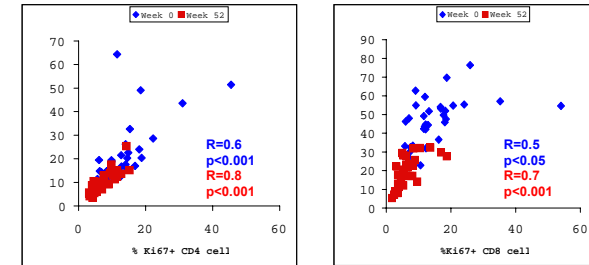


Example of histogram of Ki67 expression in CD4+ T cells

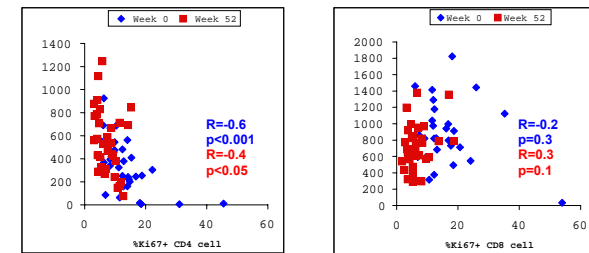
4- T cell turnover correlates with viral load both at baseline and at week 52 of HAART in both the CD4+ and CD8+ subsets.



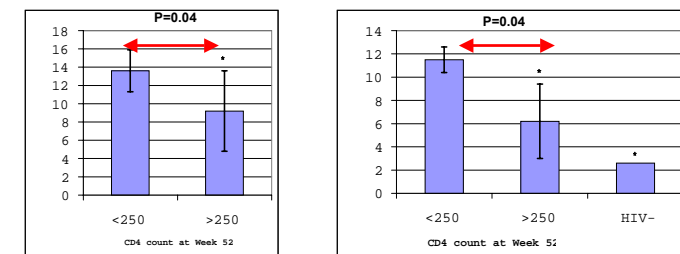
5- T cell turnover correlates with immune activation both at baseline and at week 52 of HAART in the CD4+ and CD8+ subsets.



6- T cell turnover correlates with cell counts both at baseline and at week 52 of HAART in the CD4+ but not the CD8+ subsets.



7- In patients with viral loads <50 copies/ml at week 52 of HAART, CD4+ T cell activation and turnover are significantly higher among patients who fail to achieve a CD4 count >250 cells/ul.



Conclusions

- The observed increase in turnover of CD4+ and CD8+ T cells in HIV infection is related to immune activation and does not normalize after HAART despite suppression of viral load to <50 copies/ml.
- T cell activation and T cell turnover are central to CD4 depletion in HIV infection and play an important role in the failure of CD4 recovery with HAART.