

Poster presentation

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## HIV-1 natural viral suppressors: control of viral replication in the absence of therapy

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### Background

HIV Natural Viral Suppressors (NVS) are individuals with HIV-1 that are able to suppress HIV viral replication to undetectable levels in the absence of antiretroviral therapy. By contrast, Long-Term Nonprogressors (LTNP), represent individuals who are HIV-1 infected but who maintain high CD4 counts over many years (no where in the definition of LTNPs is viral load considered, and in most series the HIV-1 viral loads range from  $10^2$  to  $10^4$  copies/ml) [1-3]. We present here a cohort of NVS, providing a case definition for identifying such individuals and the results of preliminary evaluations.

### Methods

Inclusion/Exclusion Criteria:

1. Confirmed HIV-1 by Western blot.
2. Positive HIV-1 Proviral DNA.
3. Viral loads <400 copies/ml at all time points for at least a 2 year period and 4 viral load measurements (One viral

blip or viral load > 400 copies/ml during the above time period was permitted if the subsequent viral loads were <400).

4. No more than 2 weeks of antiretroviral (ART) use (unless administered for pregnancy prophylaxis)

Studies included High Input PCR for Proviral DNA copy number.

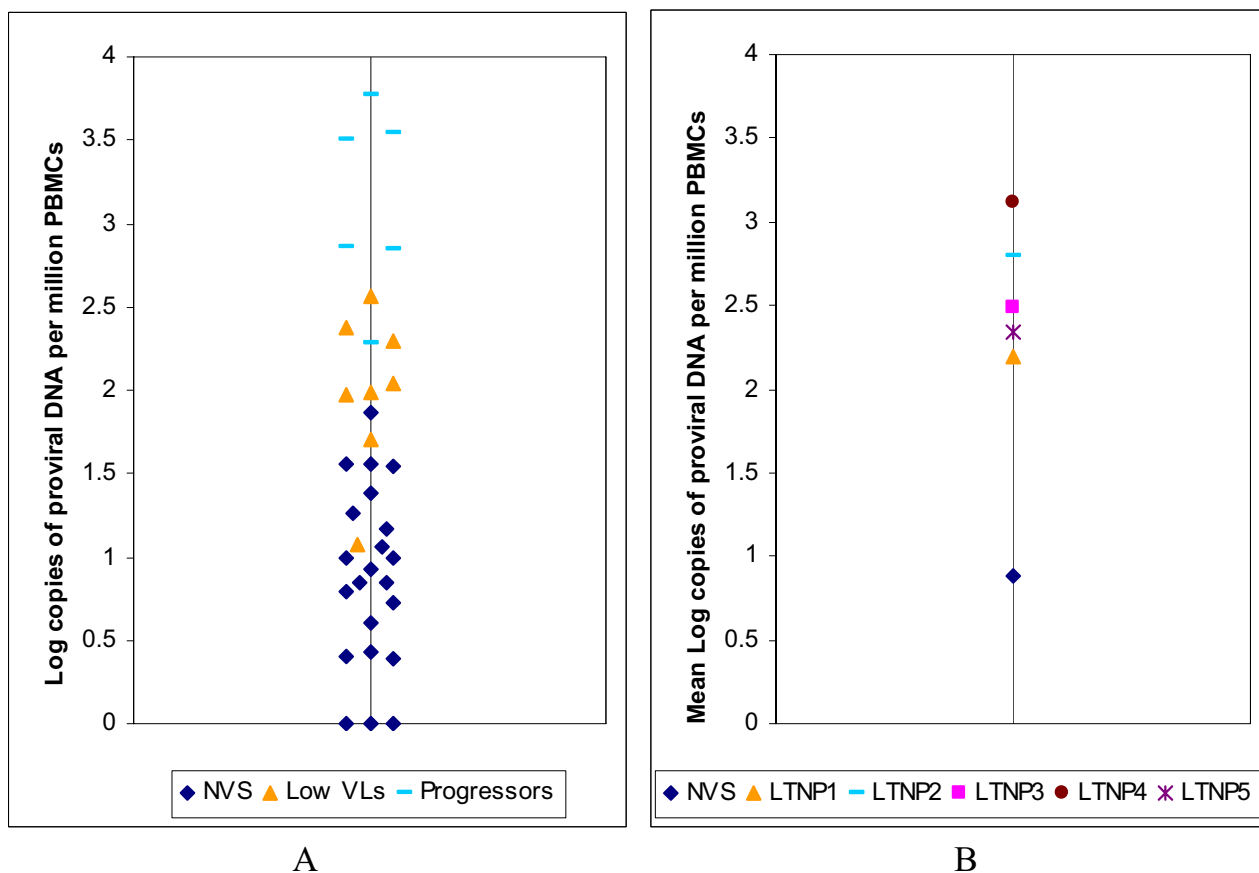
### Results

35 patients were identified as NVS, and 22 have been enrolled. Demographics are shown in Table 1.

Using a high-input assay developed specifically for this cohort (limit of detection 1 copy/ $10^6$  PBMCs), proviral DNA copy number ranged from 1–74 copies/ $10^6$  PBMCs (refer to Figure 1). The mean proviral DNA copy number was lower than both the controls we used in this study, HIV progressors and individuals with low viral loads (Figure 1A). The later group consisted of HIV infected individuals who had viral loads of 500–15,000 copies/ml, viral

**Table 1: Demographics of the NVS cohort**

Age	51 (range 38–60)
Sex	Male 64%, Female 36%
Race	African American 100%
Median years with HIV	12 (range 2–19)
Median years viral suppression	5 (range 2–9)
Median of latest CD4 count (cells/ul)	887 (range 346–1564)
Average number of viral loads tested	13 (range 4–21)



**Figure 1**  
**A** HIV-1 proviral copy numbers/ $10^6$  cells. Progressors are individuals with HIV-1 viral loads  $>100,000$  copies/ml. Low VLs are individuals with viral load of 500–15,000 copies/ml. **B** Mean HIV-1 proviral copy numbers/ $10^6$  cells of the NVS cohort compared to published data of LTNP cohorts [1,4-7].

loads that are comparable to the majority of LTNPs. Because some individuals in this group did not meet the classic definition of LTNPs, we compared the mean HIV proviral load of the NVS cohort to five published LTNP cohorts, and the NVS cohort was consistently 1 to 2 logs lower than that described in LTNPs, again confirming that individuals classified as NVS did in fact demonstrate more effective control of in vivo HIV-1 replication as reflected by quantification of HIV DNA proviral copy number.

### Conclusion

Patients with HIV-1 infection who are able to naturally suppress HIV infection in the absence of therapy represent one particular extreme of HIV infected patients. Although it is too early to postulate on the factor or factors that makes this group unique, there are likely multiple mechanisms involved in effective in vivo regulation of HIV resulting in persistent non-therapeutic induced viral suppression. The study of NVS, which represent a more homologous group than LTNP in regards to HIV-1 sup-

pression, should lead to better understanding of the immunoregulatory mechanisms involved. Studies are underway to determine and further characterize the in vivo mechanisms responsible for control of HIV-1 replication seen in Natural Viral Suppressors.

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