**BACKGROUND**

With the use of combination antiretroviral therapy (cART), prolonged viral suppression of plasma HIV-RNA levels (<40 copies/ml) is achievable in the majority of patients with HIV-1 infection. One paradoxical observation is that, despite prolonged viral suppression with no evidence of active viral replication, the majority of HIV-infected patients exhibit persistent presence of HIV-1 proviruses, persistent seropositivity to HIV-1 and evidence of immune activation. Over 90% of proviruses in the peripheral blood are thought to be "defective". As these defective proviruses are unable to encode intact virions, the peripheral blood pool of proviruses has been thought to largely represent a silent "graveyard" of viral sequences. In a single case, we previously reported the ability of a provirus with a stop codon in the protease to transcribe viral RNA. Cells harboring these "defective" proviruses were found in a clonally expanded population of CD4+ T cells that had persisted for 17 years (Imamichi H. et al., AIDS 2014, 28:1091-1099).

**OBJECTIVE**

To better characterize these defective proviruses and determine whether or not they might be biologically active, even in patients with prolonged HIV-RNA levels <40 copies/ml.

**STUDY DESIGN**

Cross-sectional study of:
- 4 virologically suppressed patients with pVL<40 copies/ml for >6 yrs (range 6.1-11.9) pVL<40 copies/ml
- 4 virologically suppressed patients with pVL<40 copies/ml for >6 yrs (range 6.1-11.9)

**RESULTS**

**BACKGROUND**

Agarose gel pictures depicting sizes of proviral DNA PCR fragments generated using the 5'LTR- to 3'LTR PCR. Only positive PCR reactions determined at limiting dilutions are shown.

Single-genome sequencing of 175 HIV-1 proviruses determined that 53% (48/90) in pVL<40 pts were defective. The majority of defective proviruses could be characterized as truncated forms with gross internal deletions (87% in pVL<240; and 93% in pVL<40).

**RESULTS**

In vivo transcription of clonally expanded "defective" proviruses (clones ii and vi) was seen in two patients (Pts 5 and 7) with pVL<40 copies/ml. Known unspliced and spliced RNA species are shown in the top panel. Only unique unspliced HIV-RNA sequences are shown. Novel unspliced HIV-RNA species that had corresponding DNA sequences are identified by lower case alphabets.

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