SUSTAINED HIGHER LEVELS OF INTRACELLULAR HIV-1 RNA TRANSCRIPT ACTIVITY IN VIRAL BLIP PATIENTS

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Background:
Virally suppressed HIV patients on antiretroviral therapy (ART) occasionally experience viral blips, or low-level elevations of HIV-1 plasma viral load. The clinical significance of blips is unclear. It has been suggested that blips may be related to HIV-1 reservoir activity. We used a new highly sensitive assay to investigate HIV-1 RNA transcriptional activity of PBMCs in patients with and without blips, and further explored production of infectious virus from the viral reservoir.

Methods:
RNA and DNA was extracted from cells in 6ml of peripheral blood, from HIV-1 patients on ART, virally supressed, with no blips (n = 52) or with one or two blips (n =55) in the previous 2 years. Follow-up samples of the patients were also studied. HIV-1 RNA transcripts and proviral DNA was measured using our assay, which targets the highly conserved "R" region of the LTR, termed as Double-R assay. Transcriptional activity and measure of replication competent virus was also analysed in activated purified CD4+ T cells.

Results:
Blip patients had significantly higher levels of HIV-1 RNA transcripts vs without blips (median 192 vs 49 copies/10^6 white blood cells; p=0.0007, range 1.3 to 5,415). The follow-up sample analysis revealed that increased levels of HIV-1 transcription were maintained in follow up samples of blip patients. This correlated well with higher levels of inducible transcripts after activation in vitro, and production of replication competent HIV-1. Three distinct patients, including an elite controller, had very low levels of transcripts with inability to induce productive infection in vitro.

Conclusion:
Viral "blips" reflect higher transcriptional activity from the reservoir despite viral suppression, and slightly higher HIV-1 DNA over time. Viral "blips" are therefore significant. This sensitive assay can be used in monitoring the size and activity of the HIV-1 reservoir and will be useful in research into HIV-1 cure strategies.

Disclosure of Interest Statement:

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