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Measurement of HIV-1 Latently Infected Cells Before and After Antiretroviral Therapy in People Living with HIV

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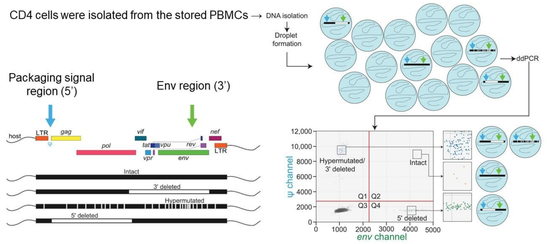
Introduction

Antiretroviral therapy (ART) is an effective treatment that suppresses the progression of infection by inhibiting HIV-1 viral replication. However, the presence of a latent HIV-1 reservoir makes it difficult to eradicate the disease. To develop a strategy for curing HIV-1 infection, it is necessary to characterize this reservoir and establish a measurement system to accurately evaluate its dynamics. In this study, we established a measurement system using a method to isolate CD4 cells from stored peripheral blood mononuclear cells (PBMCs) and then extracted DNA. We then measured latently HIV-infected cells in people living with HIV before and after ART to evaluate the dynamics of the HIV-1 reservoir.

Methods

We analyzed samples of 26 people living with HIV-1 attending our hospital who had stored PBMCs in our biobank before and after ART (when plasma viral load [VL] was <20 copies/mL). CD4 cells were isolated from the stored PBMCs, and DNA was extracted. HIV-1 latently infected cells were measured using the Intact Proviral DNA Assay (IPDA).



Results

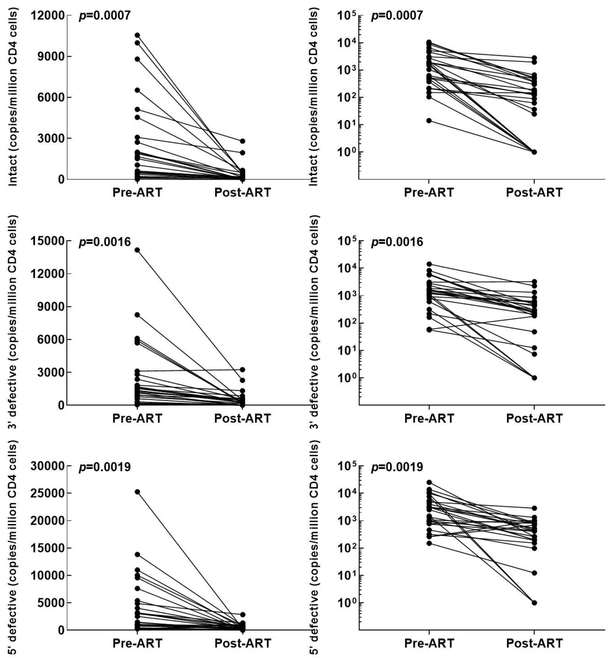


Figure 1. Measurement of HIV-1 Latently Infected Cells in Pre-ART and Post-ART. Upper: Intact; Middle: 3' defective/HM; Lower: 5' defective.

Table 1. The p-value of simple linear regression.

	Pre-ART				Post-ART			
	Pre-ART CD4	Post-ART CD4	Pre-ART VL	Number of days until VL <20 copies /ml	Pre-ART CD4	Post-ART CD4	Pre-ART VL	Number of days until VL <20 copies /ml
Intact	0.7684	0.6277	0.1473	0.1369	0.7182	0.8579	0.6449	0.9591
3' defective/HM	0.2732	0.6297	0.0632	0.0441	0.1113	0.2682	0.5593	0.5459
5' defective	0.5892	0.8504	0.0305	0.3092	0.0717	0.1096	0.1703	0.7099

Results (cont.)

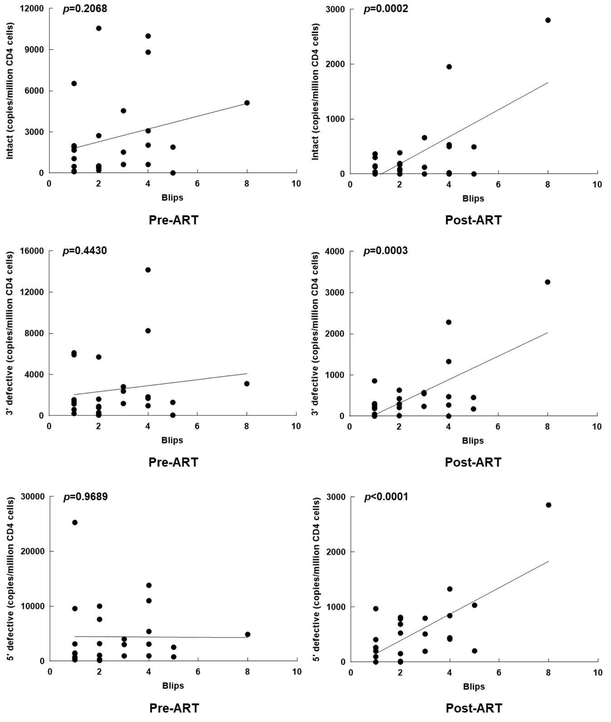


Figure 2. The correlation between the number of blips after VL <20 copies/mL and intact, 3' defective/HM, and 5' defective proviruses.

Summary

IPDA showed a significant decrease in the number of HIV-1 DNA copies per million CD4 cells after ART. This applied to intact, 3' defective/hypermutated (HM), and 5' defective proviruses (p=0.0007, p=0.0016, p=0.0019, respectively) (Figure 1). There was no significant correlation between the number of intact, 3' defective/HM, and 5' defective proviruses pre- and post-ART and pre- or post-ART CD4 cell count, pre-ART VL, or the number of days until VL <20 copies /ml was achieved (Table 1). There was also no significant correlation between the number of blips after VL <20 copies/mL and intact, 3' defective/HM, and 5' defective proviruses before ART, but a significant correlation was observed for them after ART (p=0.0002, p=0.0003, p<0.0001, respectively) (Figure 2).

Conclusions

These results suggest that the number of blips after VL < 20 copies/mL was significantly correlated with the numbers of copies of intact, 3' defective /hypermutated, and 5' defective proviruses per million CD4 cells after ART, suggesting that HIV latently infected cells at VL < 20 copies/mL can be an indicator of subsequent blips.

Reference

Simonetti FR, et al. Intact proviral DNA assay analysis of large cohorts of people with HIV provides a benchmark for the frequency and composition of persistent proviral DNA. PNAS 117: 18692-700, 2020.