Similar Intact and Defective HIV Provirus Frequency in Suboptimal Immune Responders and Controls

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BACKGROUND

- A significant percentage of people living with HIV (PWH) who initiate antiretroviral therapy (ART) with low CD4+ T cell counts have CD4+ T cell counts that rise slowly or plateau at low levels despite viral suppression. One term for individuals who experience this is suboptimal immune responder (SoIR).
- A correlation between the frequency of HIV-infected CD4s and low CD4 counts on ART has been reported. However, these studies did not control for CD4 nadir nor time on ART.
- It remains unclear whether SoIRs have a higher burden of HIV-infected CD4+ T cells or a larger HIV reservoir than others with robust CD4 count trajectories.

OBJECTIVE

- To compare the frequency of intact and defective HIV proviruses in the first few years after ART initiation in SoIRs and matched controls who start/restart on ART with CD4+ T cell counts < 200 cells/mm ^{3}.

METHODS

- Cryopreserved PBMCs were obtained from 62 SoIRs and 67 controls at one time point 1-5 years post-ART initiation.
- All participants initiated ART with a CD4 count < 200 cells/mm ^{3} and maintained virologic suppression for > 5 years.
- SoIRs were defined as PWH with a CD4 count <350 at 5 years post-ART initiation. Controls were defined as PWH with a CD4 count >500 at 5 years post-ART initiation.
- Groups were matched on age, race, sex, CD4+ T cell nadir, hepatitis C serostatus, ever-IV drug use, and time from ART initiation to sample collection.
- Samples and clinical data were sourced from four cohorts: ALLRT/ACTG (n=76), the SCOPE cohort (n=46), the Cleveland Immune Failure cohort (n=7), and the Johns Hopkins HIV Clinical Cohort (n=1).
- CD4+ T cells were isolated from PBMC samples and the intact proviral DNA assay (IPDA) was used to quantify frequency of intact and defective HIV proviruses among CD4+ T cells. The average of ~5 replicates per sample-timepoint was used.

The frequency of intact and defective HIV proviruses in CD4+ T cells is similar in suboptimal immune responders (SoIRs) and people with robust CD4 responses.

RESULTS

Table 1. Participant characteristics.

	SoIR (n=62)	Control (n=67)
Age at ART start/restart (y), median (IQR)	45 (40-50)	42 (37-47)
Female sex at birth, no (%)	6 (10%)	10 (15%)
White race, no (%)	39 (63%)	38 (57%)
Black/African American race, no (%)	15 (24%)	19 (28%)
Hepatitis C seropositive, no (%)	9 (15%)	10 (15%)
Reported ever IV drug use, no (%)	13 (21%)	12 (18%)
CD4+ T cell nadir, median (IQR)	29 (11-61)	31 (14-90)
CD4 count at ART start/restart, median (IQR)	53 (19-104)	50 (20-131)
CD4 count 5 years after ART initiation, median (IQR)	265 (210-308)	650 (560-794)
Months between ART start/restart and sample, median (IQR)	22 (19-32)	22 (20-30)
Cohort – no (%)		
ALLRT/ACTG	27 (44%)	49 (73%)
SCOPE	27 (44%)	18 (27%)
CLIF	7 (11%)	0
JHHCC	1 (2%)	0

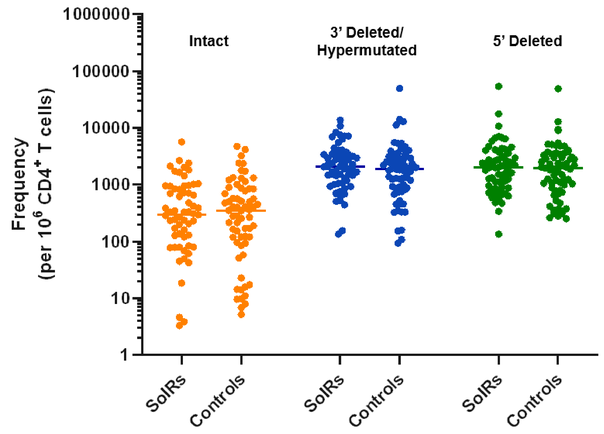


Figure 1. Intact and defective provirus frequency per million CD4+ T cells in suboptimal immune responders (SoIRs) and PWH controls matched for age, race, sex, CD4+ nadir, HCV serostatus, ever-IV drug use, and time from ART start/restart to sample collection. Horizontal bars represent medians. No comparison between groups is significant.

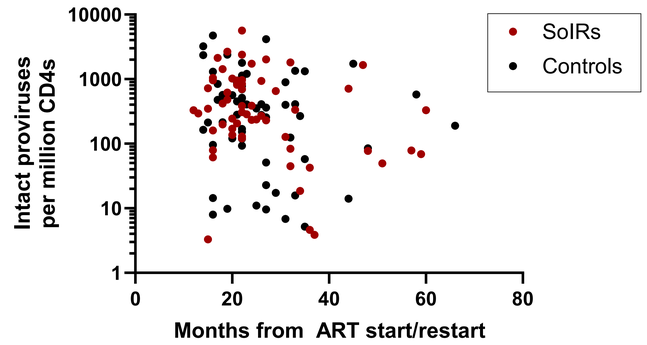


Figure 2. Intact provirus frequency per million CD4+ T cells in SoIRs (red) and controls (black) plotted by months between ART start/restart and sample collection. No significant correlation between intact provirus frequency and months on ART was found in either group.

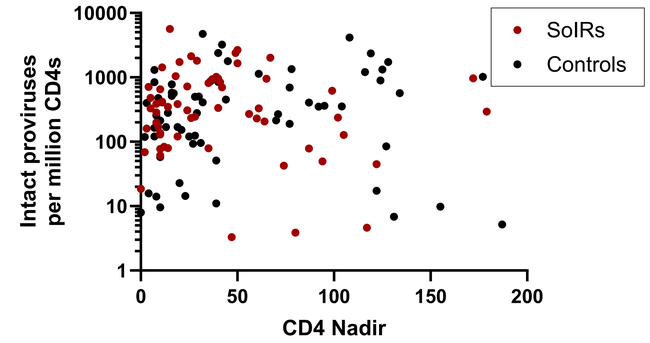


Figure 3. Intact provirus frequency per million CD4+ T cells in SoIRs (red) and controls (black) plotted by CD4 nadir. No significant correlation between intact provirus frequency and CD4 nadir was found in either group.

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