BACKGROUND

Despite remarkable advances in prevention of vertical HIV transmission and antiretroviral drug development, pediatric HIV-1 infection remains a frequent and difficult-to-treat disease. Early initiation of antiretroviral therapy (ART) in neonates infected with HIV-1 may limit the frequency and stability of HIV-1 reservoir cells, possibly improving response to interventions aimed at viral eradication and cure.

METHODS

37 children from the Early Infant Treatment cohort in Botswana, who started ART at a median of 2 days from birth, were included in this study. HIV-1 near full-length genome sequencing of individual proviral species was used to characterize the proviral reservoir landscape. Integration sites associated with each proviral sequence were obtained using Matched Integration site and Proviral Sequencing (MIP-Seq). Immune responses were measured using flow cytometry.

RESULTS

I. Proximal DNA levels decreased by 5-10 fold after 84-96 weeks of early and continuous treatment; with more significantly pronounced decrease for intact compared with defective HIV-1 proviruses

II. In two study participants, intact proviruses at week 84 were frequently integrated in heterochromatin regions that represent atypical sites for proviral integration during primary infection.

III. At birth, the frequency of intact proviruses was inversely associated with IL-8-secreting CD4 T cells (Th8), which represent a dominant cell subset in neonates and displayed higher levels of cell-intrinsic resistance to HIV-1 infection.

CONCLUSIONS

Together, these results suggest that HIV-1 reservoir cell seeding and evolution in early-treated children is markedly influenced by innate immune responses.