ABSTRACT

HIV-1 escapes by acquiring mutations that differentially influence the course of infection. Unlike HIV-1 structural and enzymatic proteins, it remains elusive what extent the host immune-mediated selection pressure influences the variability of the accessory (Vif, Vpu, Vpr, and Nef) and regulatory (Tat and Rev) proteins. To address this, we analyzed the viral sequences encoding accessory and regulatory proteins from 446 human leukocyte antigen (HLA)-typed, chronically HIV-1 subtype B-infected, and treatment-naive individuals in Japan. We observed that Vpu and Vpr were the most and least polymorphic proteins with the average Shannon entropy scores of 0.63 and 0.38, respectively. Phylogenetically corrected methods identified a total of 161 HLA-associated polymorphisms; whereby Nef and Vpu had the highest (26.6%) and lowest (1.2%) proportion of amino acid sites associated with HLA-class I alleles, respectively. These results add further insight on the role of HLA-mediated selection pressure on HIV-1 sequence polymorphisms of HIV-1 accessory and regulatory proteins.