HIV CNS COMPARTMENTALIZATION AMONG SUBJECTS WITH HIV-1 SUBTYPES G AND CRF02_AG

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Background

HIV-1 compartmentalization in the central nervous system (CNS) and its contribution to neurological disease are incompletely understood. Previous studies were conducted among subjects infected with subtypes B or C. Little is known about other HIV-1 subtypes. We investigated HIV-1 compartmentalization in the CNS of subjects infected with HIV-1 subtypes G and CRF02_AG, the most prevalent subtypes in West Africa.

Methods

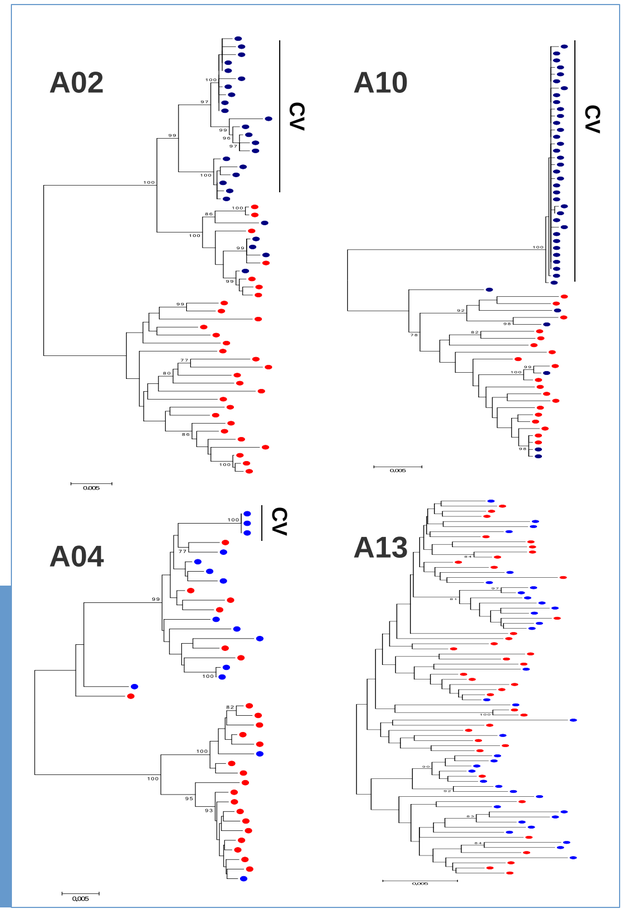
A cross-sectional study was conducted among HIV-infected subjects with suspected cryptococcal meningitis at Jos University Teaching Hospital, Nigeria. Paired plasma and cerebrospinal fluid (CSF) samples were collected from 13 (M-6, F-7; age range: 23-45yrs) subjects with a clinical indication for lumbar puncture. Viral RNA extraction, cDNA synthesis, and amplification of the V1/V3 region of *env* and the full-length HIV-1 *env* gene were done by PCR techniques using specific sets of primers. Pooled libraries of VI/V3 amplicons (tagged with Primer ID) and full length HIV *env* genes were analyzed by deep sequencing and single genome amplification (SGA) assays respectively, followed by phylogenetic analysis to determine evolutionary association.

Results

Plasma and CSF viral RNA of the subjects ranged between <400 - 1.0 x10^6 copies/mL and <400 - 5.1 x10^6 copies/mL, respectively. Six of the subjects had sufficient levels of virus in the CSF to allow comparison to virus in the blood. All recovered isolates were most closely related to HIV-1 subtypes G or CRF02_AG. Deep sequencing demonstrated HIV-1 compartmentalization in the CNS in subjects A02, A04 and A10, equilibrated virus populations in the plasma and CSF in subject A13, and no evidence of compartmentalization in subjects A05 and A12. Further analysis by SGA assay confirmed the findings and showed a diverse level of compartmentalization in the subjects (Figure 1). Determination of the method of entry of the compartmentalized variants is ongoing.

Figure 1. Phylogenetic trees of **plasma** and **CSF** HIV-1 SGA *env* sequences of 4 subjects infected with HIV-1 subtype AG. **Plasma** and **CSF** sequences are in **red** and **blue**, respectively. Subject A2, A4, and A10 contain compartmentalized variants (**CV**). Subject A13 had equilibrated viral population. The HIV-1 viral loads of plasma and CSF of the 4 subjects are listed blow.

	A02	A04	A10	A13
Plasma VL	27,456	162,544	439,512	1,073,000
CSF VL	3,656	2,104	554,088	5,107,488



Conclusions

- First documentation of CNS compartmentalization of HIV-1 subtypes G and CRF02_AG.
- Improved understanding of effects compartmentalization on CNS HIV drug susceptibility, viral reservoir, and neurological disorders in sub-Saharan Africa where these subtypes are dominant is imperative.
- Extremely high viral RNA levels observed in the CSF of subject A13 may be due to the transfer of infected T cells into the CSF/CNS.

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