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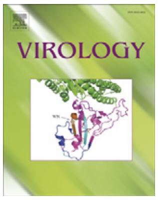

Phylodynamic analysis of the dissemination of HIV-1 CRF01_AE in Vietnam

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ABSTRACT

To estimate the epidemic history of HIV-1 CRF01_AE in Vietnam and adjacent Guangxi, China, we determined near full-length nucleotide sequences of CRF01_AE from a total of 33 specimens collected in 1997–1998 from different geographic regions and risk populations in Vietnam. Phylogenetic and Bayesian molecular clock analyses were performed to estimate the date of origin of CRF01_AE lineages. Our study reconstructs the timescale of CRF01_AE expansion in Vietnam and neighboring regions and suggests that the series of CRF01_AE epidemics in Vietnam arose by the sequential introduction of founder strains into new locations and risk groups. CRF01_AE appears to have been present among heterosexuals in South-Vietnam for more than a decade prior to its epidemic spread in the early 1990s. In the late 1980s, the virus spread to IDUs in Southern Vietnam and subsequently in the mid-1990s to IDUs further north. Our results indicate the northward dissemination of CRF01_AE during this time.

Introduction

HIV-1 infection in Vietnam was first documented in a young woman who was presumably infected by her foreign partner in late 1990 in Ho Chi Minh City (Lindan et al., 1997). By the early 1990s, HIV-1 had spread slowly among female commercial sex workers (fCSWs) and their clients. However, in 1993, an HIV-1 epidemic broke out among injecting drug users (IDUs) in Khanh Hoa Province and Ho Chi Minh City in Southern Vietnam (Subcommittee, 1998). By the end of 2005 the epidemic had spread to Northern Vietnam (UNAIDS/WHO, 2006a). Between 2000 and 2007, the estimated number of people living with HIV in Vietnam more than doubled from 122,000 to 290,000, and approximately 40,000 Vietnamese are estimated to be infected with HIV each year (UNAIDS/WHO, 2008).

CRF01_AE is almost the sole HIV-1 strain circulating in Vietnam, in all geographical regions and risk populations (Lan et al., 2003; Osmanov et al., 2002; Weniger et al., 1994). Only a few cases of HIV-1 subtype B infection have been reported so far (including the first Vietnamese case reported in 1990) (Kato et al., 1999; Menu et al., 1996). Previous studies, including ours, have identified genetic differences among HIV-1 CRF01_AE strains sampled from different locations and risk populations (Beyrer et al., 2000; Kusagawa et al., 1999; Nerurkar et al., 1996; Yu et al., 1999), and the similarity of viruses circulating among IDUs in Northern Vietnam and the nearby Guangxi Province of China suggests the cross-border transmission of CRF01_AE (Kato et al., 2001, 1999; Piyasirisilp et al., 2000).

In this study, we investigated the timescale and epidemic history of CRF01_AE transmission in Vietnam and neighboring locations, using established phylogenetic and evolutionary analysis methods.

Results

Phylogenetic characteristics of CRF01_AE isolates from Vietnam

A total of 33 near full-length nucleotide sequences (HXB2: 790–8795) representing CRF01_AE infections from Vietnam were subjected to phylogenetic analysis together with available reference sequences. The similarity between Vietnamese isolates and each subtype was calculated by Simplot analysis. The Vietnamese isolate (97VNHD10) showed greatest similarly with CRF01_AE (CM240), and this was confirmed by bootscanning analysis. One representative result (for 97VNHD10, which belongs to cluster 3) is shown in Figs. 1B and C. The recombination analysis results of other Vietnamese isolates were similar to those shown in Figs. 1B and C (data not shown). These results indicate that Vietnamese isolates obtained in the present study are CRF01_AE without evidence of further recombination events. Maximum likelihood trees revealed that all of the Vietnamese and Guangxi CRF01_AE sequences (except three) grouped as a single monophyletic cluster within the Thai isolates (Fig. 1A). The Vietnamese sequence group is composed of three distinct clusters (Fig. 1A

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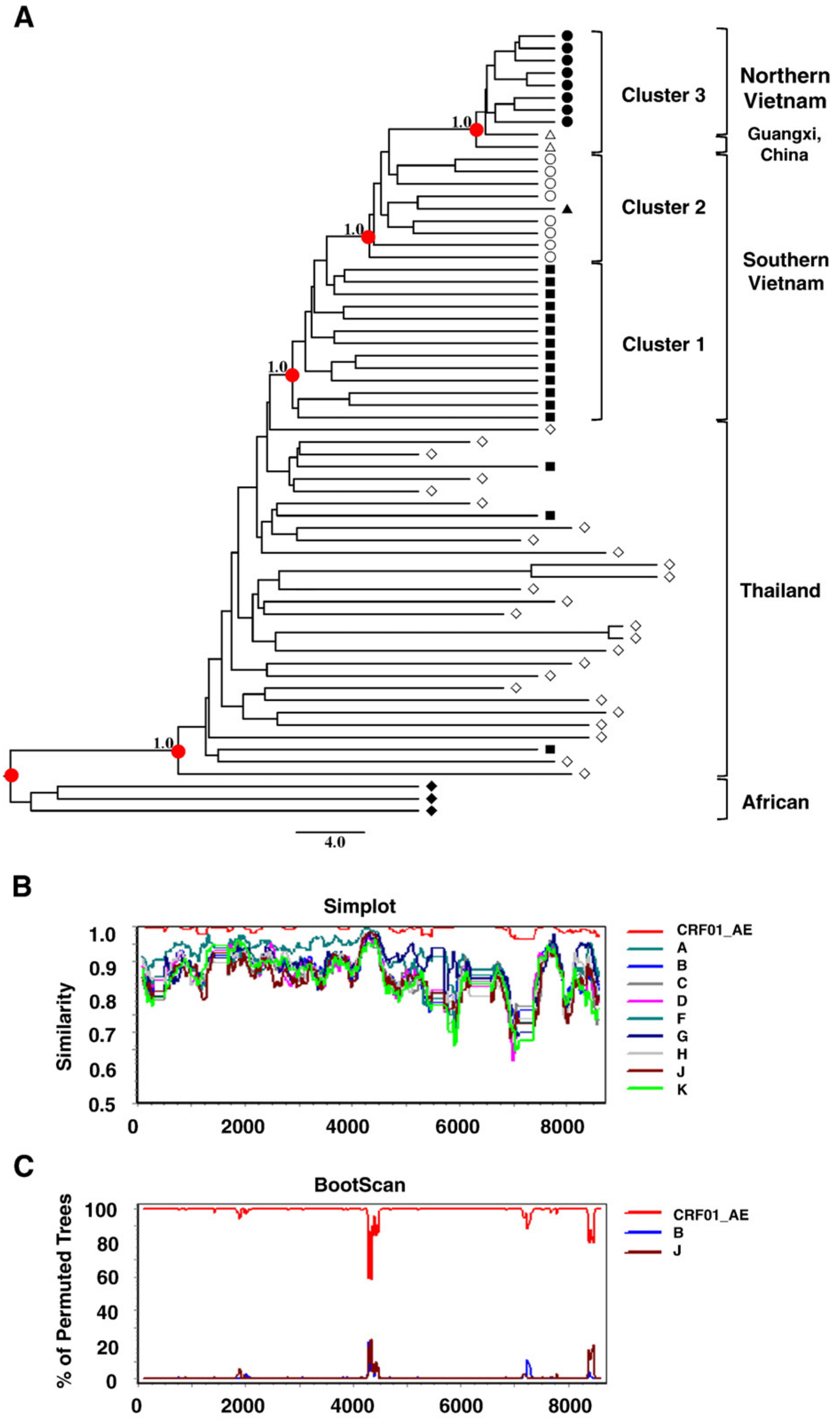

Fig. 1. HIV-1 CRF01_AE strains from Vietnam grouped into three distinct clusters. (A) Maximum clade credibility (MCC) tree of near full-length HIV-1 CRF01_AE isolates obtained by Bayesian MCMC analysis (see Materials and methods for details). Symbols represent different locations and risk groups: ♦ = African CRF01_AE; ◊ = Thailand CRF01_AE; ■ = heterosexuals in Southern Vietnam; ○ = IDU in Southern Vietnam; ● = IDU in Northern Vietnam; ▲ = heterosexuals in Northern Vietnam; △ = IDU in Guangxi Province of China. Posterior probabilities are indicated for each cluster. Scale bar is years. (B) The similarity between the Vietnam isolates and the references were plotted using Simplot program. (C) The recombination analysis of each Vietnamese isolate was performed by BootScan within SimPlot program. The reference subtypes are indicated in the box.

and Supplemental Fig. S1). Cluster 1 ($n = 13$) is paraphyletic and exclusively contains sequences from heterosexuals in Southern Vietnam. Cluster 2 ($n = 9$) is paraphyletic and contains sequences from IDUs in Southern Vietnam ($n = 8$) plus one sequence from a Northern Vietnamese STD patient (98VNND15). Cluster 3 ($n = 10$) is monophyletic and contains sequences from IDUs in Northern Vietnam ($n = 8$) and the nearby Chinese province of Guangxi ($n = 2$). The only exceptions that did not belong to these clusters are 3 specimens from