

First Appearance of HIV-1 CRF07_BC and CRF08_BC Outside China

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Abstract

Neither full length genomic sequence of CRF07_BC nor that of CRF08_BC was found in any other countries since they originated in Yunnan, China, in early 1990s. Here, we first report that CRF07_BC and CRF08_BC appeared among intravenous drug users in Shan state of Myanmar bordering Yunnan, and confirmed that they spread from China to Myanmar. The introduction of CRF07_BC and CRF08_BC in northern Myanmar may forebode a changing subtype epidemic in Southeast Asia.

Keywords: human immunodeficiency virus, CRF07_BC, CRF08_BC, intravenous drug user, Myanmar

HIV-1 CIRCULATING RECOMBINANT FORMS (CRFs) are common where multiple subtypes cocirculate. During past two decades, a large number of HIV-1 CRFs were formed among intravenous drug users (IDUs) in China.¹ In particular, CRF07_BC and CRF08_BC originated in Yunnan in 1993 and 1990, respectively, and then spread to other regions of China through drug-trafficking routes.^{2,3} Currently, CRF07_BC has become the most common HIV-1 subtype circulating in China after spreading to individuals with sexual risk.⁴ In 2003, CRF07_BC was identified in Taiwan⁵ with a likely migration between 1998 and 2001 (Fig. 1A). Interestingly, neither full length genomic sequence of CRF07_BC nor that of CRF08_BC was found in any other countries. Surveillance for these CRFs outside China could help us understand migration of risk groups and identify opportunities for prevention.

During November 2013 to November 2014, we obtained 26 near full-length HIV-1 genomic sequences from 31 HIV-1-positive blood samples from IDUs in detoxification centers in Shan State, Myanmar. Two CRF08_BC and one CRF07_BC strains were detected by phylogenetic analysis and confirmed by bootscan analyses (Fig. 1B, C). Although CRF07_BC and CRF08_BC originated in Yunnan in early 1990s, these CRFs were rarely found in Yunnan's Dehong prefecture, and not previously identified in northern Myanmar.^{1,6,7} This is the first report that CRF07_BC and CRF08_BC appeared in Myanmar despite sharing the same risk population, that is, IDUs, in bordering Yunnan, China. Bayesian phylogeographic analysis showed that the CRF07_BC strain more likely spread from

Xinjiang province of China to Myanmar possibly through Yunnan after 1996,⁸ and the CRF08_BC strains spread from Yunnan province to Myanmar after 1992 (Fig. 1A, D).³

These results may suggest a new HIV prevention challenge in the China–Myanmar border region. The increasing prevalence of CRF07_BC in China and now Myanmar implies it may have high-transmission potential, which is supported by the large outbreak of CRF07_BC occurring in Taiwan in 2003, occurring only 2–5 years after its introduction from mainland China.⁵ Although the appearance of CRF07_BC and CRF08_BC in northern Myanmar does not imply an outbreak in the future, it will increase the subtype complexity of the HIV epidemic in Myanmar and may lead to the formation of more complicated recombinant forms (e.g., second-generation recombinants between CRF07_BC/CRF08_BC and other subtypes) of HIV strains in this region.^{9–13} Furthermore, Myanmar plays a crucial “hub” for HIV-1 transmission across several Southeast Asian countries¹⁴; therefore, once CRF07_BC and CRF08_BC have established epidemics in Myanmar, there is a high possibility of spreading from Myanmar to other Southeast Asian countries through drug trafficking and other high-risk routes, which may change the HIV epidemic patterns in the region. Taken together, our observations suggest that the introduction of CRF07_BC and CRF08_BC in northern Myanmar may forebode a changing subtype epidemic in Southeast Asia, and further molecular surveillance is warranted.

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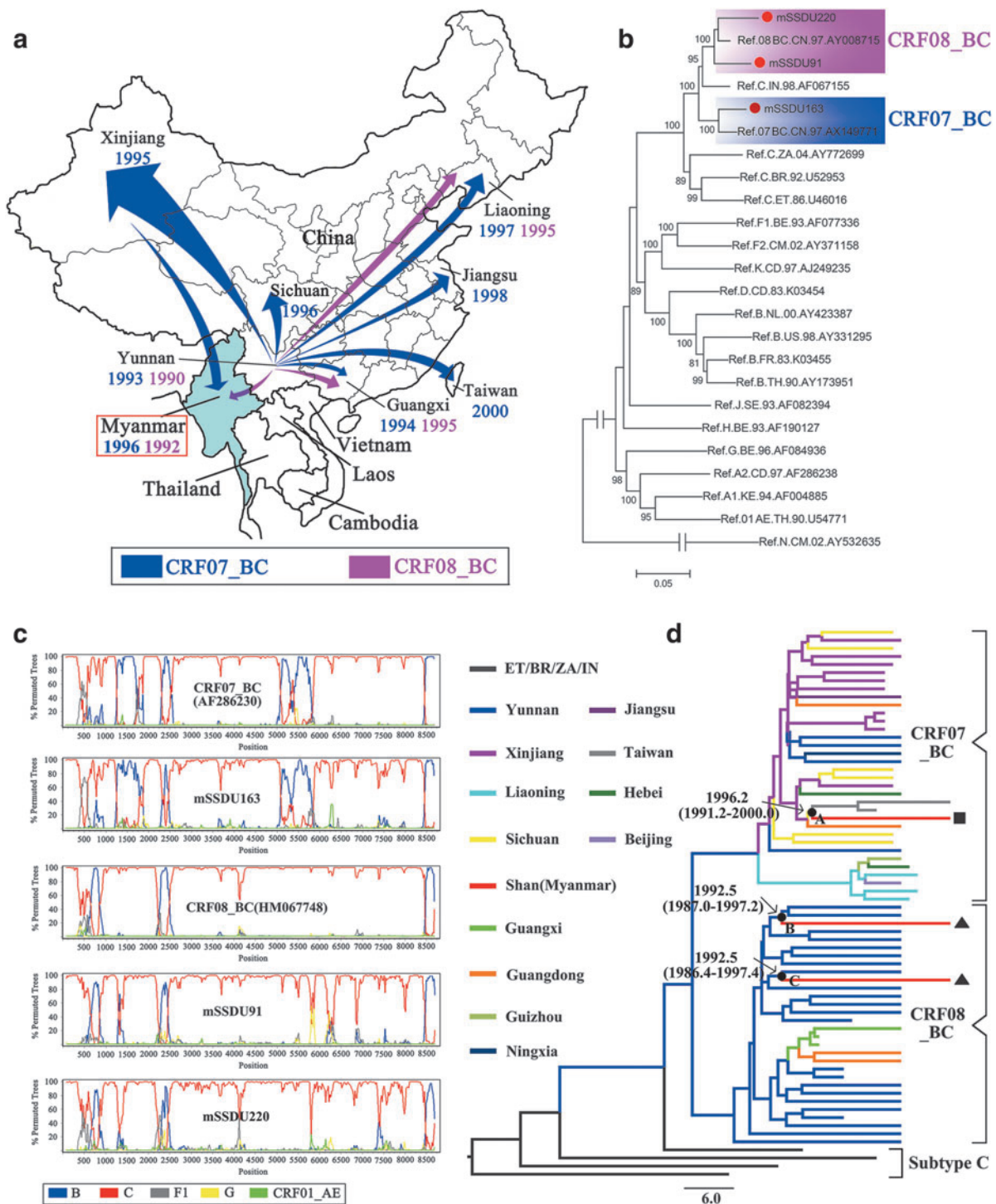


FIG. 1. Phylodynamics of CRF07_BC and CRF08_BC in north Myanmar. **(a)** Transmission dynamics of CRF07_BC and CRF08_BC in Asia. *Blue and magenta arrows* indicate the migration routes of CRF07_BC and CRF08_BC in different countries/provinces, respectively. **(b)** Maximum-likelihood tree of three HIV-1 strains from Shan state of Myanmar. Subtype references include N group (used as outgroup), M group subtypes A-K, CRF01_AE, CRF07_BC, and CRF08_BC. The support of each branch, as determined from 1,000 bootstrap samples, is indicated by the value at each node, and only bootstrap values more than 75% are shown. **(c)** Bootscanning plots of CRF07_BC and CRF08_BC strains from Myanmar. Bootscanning plots are constructed by using Simplot 3.5 .1 software based on 100 replicates with a 200-bp sliding window moving in steps of 20 bases. Subtype references include B' (AY173951), C (AF067155), F1 (AF077336), G (AF084936), and CRF01_AE (U54771). **(d)** Maximum clade credibility tree of CRF07_BC and CRF08_BC in Asia. The longest mutual region of subtype C origin (3311-5700nt according to HXB2) is selected for Bayesian phylogeographic analysis. All near full-length sequences of CRF07_BC and CRF08_BC with sampling time and location, and pure subtype C sequences from Brazil (BR, U52953), Ethiopia (ET, U46016), India (IN, AF067155), and South Africa (ZA, AY772699) were downloaded from HIV sequence database (www.hiv.lanl.gov), and subjected to the phylogeographic analysis together with the CRF07_BC and CRF08_BC sequences from Myanmar. *Black square and triangles* indicate CRF07_BC and CRF08_BC newly detected in Myanmar, respectively. Original time for each node (*black dots*) is shown with 95% confidence interval. CRF, circulating recombinant form.

Sequence Data

The sequences of one CRF07_BC and two CRF08_BC identified in Myanmar are available in GenBank under accession numbers KU820832, KU820840, and KU820846.

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Author Disclosure Statement

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