

Results: NP1623 has an E gp120 and a B gp41 and was neutralized by both B and E sera. In contrast, the CRF 15 isolates have a predominantly B envelope and were neutralized most potently by B sera. In the IC p24 assay, the neutralization of CRF 15 isolates was evident in the ability of the NAb to block CD4 down-regulation, not p24 production. Using a CD4 monoclonal Ab (CD4-v4) that binds outside of the CD4/gp120 domain, the apparent CD4 down-regulation was not due to free envelope binding to CD4. While NP1623 used CCR5 and was inhibited by RANTES, the CRF 15_01/B isolates used CXCR4 (X4), but were not blocked by AMD3100 (an X4 receptor agonist). In contrast to other SI/X4 isolates, infection of CD4+ PBMC by X4 CRF 15 viruses appears to be enhanced more than one log by AMD3100.

Conclusions: The neutralization profiles of AE/B recombinants are complex and may be influenced by determinants in both gp120 and gp41. The enhancement of CRF 15_01/B isolates by AMD3100 implies a novel env-CD4-coreceptor interaction that may be influenced by their ability to down-regulate CD4. Characterization of the biology of HIV-1 recombinants with mosaic envelopes will provide important information for developing vaccine and therapeutic strategies for Southeast Asia and other regions where multiple subtypes co-circulate.

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THE CHANGING MOLECULAR EPIDEMIOLOGY OF HIV TYPE 1 AMONG NORTHERN THAI DRUG USERS, 1999 TO 2002

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CRF01_AE and subtype B have dominated the HIV-1 epidemic in Thailand since 1989. We reported a new circulating recombinant form of HIV-1, CRF15_01B, as well as other unique CRF01_AE/B recombinants among prevalent HIV infections in Thailand. We sought to study this challenging molecular picture through assessment of subtypes among recent HIV-1 seroconverters in northern Thai drug users. A total of 847 HIV-1 seronegative drug users (342 IDU and 505 non-IDU) were enrolled, from 1999 to 2002, in a prospective study; 39 HIV-1 incident cases were identified and characteristics were collected. The overall HIV-1 incidence rate was 2.54/100PY, but it was 10.0/100PY among male IDU. HIV was strongly associated with injection history; 38 of 39 seroconverters gave a history of IDU. A near full-length genome of HIV-1 was recovered by PCR amplification and sequenced from peripheral mononuclear cell extracted DNA of 38 seroconverters. Phylogenetic analysis revealed that 33 (86.8%) were CRF01_AE and 5 (13.2%) were CRF01_AE/B recombinants. These recombinants had different structure but shared some common breakpoints, indicating an ongoing recombination process. Recombinant infection increased with year of sampling (0 to 57.1%). The molecular epidemiology of HIV-1 among drug users in northern Thailand has thus entered a new era. CRF01_AE remains predominant while pure subtype B is becoming rare, and now a substantial component of the epidemic. These findings support the need for CRF01_AE and subtype B components in clade-matched vaccine strategies for Thai phase III trials. Ongoing molecular surveillance of circulating HIV-1 strains is imperative for the evaluation of HIV vaccine efficacy.

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