Molecular cloning and characterization of viruses isolated from chimpanzees with pathogenic human immunodeficiency virus type 1 infections.

Abstract:

We have previously described the development of AIDS in a chimpanzee (C499) infected with human immunodeficiency virus type 1 (HIV-1) and the subsequent pathogenic HIV-1 infection in another chimpanzee (C455) transfused with blood from C499 (F. J. Novembre et al., J. Virol. 71:4086-4091, 1997). In the present study, two virus isolates were derived from these animals: HIV-1JC from peripheral blood mononuclear cells (PBMC) of C499, and HIV-1NC from plasma of C455. These virus isolates were used to generate two infectious molecular clones, termed HIV-1JC16 and HIV-1NC7 (JC16 and NC7, respectively). Comparative analyses of the sequences of the two clones showed that they were highly interrelated but distinct. Based on heteroduplex mobility assays, JC16 and NC7 appear to represent dominant viruses in the uncloned stock population. Compared with amino acid sequences of the parental viruses HIV-1SF2, HIV-1LAV-1b, and HIV-1NDK, JC16 and NC7 showed a number of differences, including insertions, deletions, and point mutations spread throughout the genome. However, insertion/deletion footprints in several genes of both JC16 and NC7 suggested that recombination between SF2 and LAV-1b could have occurred, possibly contributing to the generation of a pathogenic virus. Comparative in vitro analyses of the molecular clones and the uncloned stocks of HIV-1JC and HIV-1NC revealed that these viruses had strikingly similar replicative abilities in mitogen-stimulated PBMC and in macrophages. Compared to the SF2 and LAV-1b isolates of HIV-1, HIV-1JC and HIV-1NC isolates were more similar to LAV-1b with respect to the ability to replicate in mitogen-stimulated PBMC and macrophages. These viruses should prove to be useful in mapping determinants of pathogenesis