

ABSTRACT

Molecular characterisation and drug resistance determination of the HIV-1 infected population in Barbados

Marquita Vernescia Gittens

To understand the emergence of HIV-1 variants and their potential impact on transmission of HIV-1 in Barbados, 36 Barbadian subtype B sequences were characterized and compared with sequences from Brazil, Argentina, Puerto Rico, United States, Spain, Lebanon, Uganda, Thailand, Trinidad, France, Belgium, Slovak Republic, Great Britain, Switzerland, Norway, Sweden, Netherlands, Lithuania, Martinique and Cuba.

Analysis of *env* c2v3c4 and *pol* protease (PR) gene regions at the DNA and protein levels documented that the majority of Barbadian subtype B strains differed significantly from the global sequences. Trinidad, Great Britain, Sweden, Slovak Republic, Lithuania, Brazil, North America, Lebanon or Puerto Rico formed possible clusters of epidemiologically linked events with Barbadian patients. Phylogenetic analysis revealed Barbadian subclusters: threonine deletion at position 13 of the V3 loop was identified in 13/36 (36%) of Barbadian *env* sequences, a feature globally found in less than 0.5% of HIV-1 sequences. The Barbadian consensus PR amino acid sequence differed from the worldwide consensus at three positions: 41 (R →K), 72 (I →?) and 77 (V →I).

The protease and reverse transcriptase region of the polymerase gene were amplified to detect the presence of inherent resistance mutations within the population of antiretroviral-naïve patients. The amino acid (aa) mutational patterns associated with drug resistance in 27 drug-naïve Barbadian individuals were evaluated. Only one RT sequence carried dual mutations at positions M41I, and T215Y, contrasting with the PR sequences, in which 24 (89%) contained at least one

inhibitor-associated mutation at positions R8Q, M36I, R57K, D60E, L63P, H69K, A71T, V77I or N88S. Of these 24, (52%) carried dual and 3 (15%) carried triple mutations. The majority of the mutations were associated with AA positions V77I (67%), L63P (63%) or D60E (18.5%) and indicated that the prevalence of 77I substitution (nelfinavir resistant) was four times higher in the Barbadian PR sequences than the worldwide prevalence of 19%.

The high variation found in the Barbadian sequences reflects cases of multiple independent introductions from outside the country. These findings suggest HIV-1 transferral from Europe or North America to the Caribbean. Barbadian HIV-1 sequences exhibit more variation than the global pool would suggest.

Keywords: Marquita Vernescia Gittens; Human Immunodeficiency virus (HIV); Barbados; distinctive subtype B