THE GLOBAL SPREAD OF SUBTYPES AND INTER-SUBTYPE RECOMBINANT HIV 1

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Abstract

The identification of globally prevalent HIV 1 strains is an important element of HIV 1 diagnosis, therapy, and prevention. Full-length genome sequencing of HIV 1, coupled with new techniques for identification and mapping of recombinant genomes, has led to new information about prevalent strains, their evolution, and their global spread.

METHODS: HIV 1 virus isolates from Asia and Africa have been studied by PCR amplification of full-length genomes using DNA from virus cultures on primary PBMC. Sequences were derived from molecular clones or by direct sequencing of PCR products with template dilution in the first round PCR to limit the complexity of the sample. Cycle sequencing with fluorescent dye terminators and an Applied Biosystems DNA sequencer were employed. Sequences were aligned with Clustal and phylogenetic analysis was with Neighbor Joining or Maximum Parsimony, with the bootstrap. Recombinant genomes were identified and mapped by distance scanning and by bootscanning, with parsimony using a sliding window of 300 nt advanced in 20nt increments.

RESULTS: Many new full length genomes of subtype A and subtype A-containing recombinants have been derived recently. Phylogenetic analysis indicates that, in addition to genetic subtypes A, B, C, D, E, F, G, H, and I, two inter-subtype recombinant forms are prevalent: an A/E recombinant in Southeast Asia and Central Africa, and A/G recombinants like the prototype IbNG from Nigeria. Many different A/C and A/D and A/G recombinants have also been found, but each is from a single individual and without evidence of epidemic spread at present. The subtype A portions of the non-recombinant subtype A viruses, of the A/E recombinants, and of the A/G-IbNG recombinants, respectively, each forms a significant subcluster within subtype A, indicating different subtype A parents for the two recombinant forms, which also differ from the current non-recombinant A viruses. The non-recombinant A viruses have been recovered exclusively from East Africa, while the A/E recombinants are from Cameroon and Central African Republic and the A/G-IbNG recombinants are largely from West and West Central Africa. This geographic separation of the genetic sub-lineages within subtype A is suggestive of separate origin, by recombination with E or G viruses in two of the three lineages, and limited geographic spread of each sub-lineage within Africa.

DISCUSSION: The contribution of recombination to the evolution of HIV 1 is substantial. In addition to the subtypes, certain recombinants have undergone epidemic spread and geographic dispersal, perhaps at different times in the history of the epidemic. Unique recombinant forms, such as the A/C and A/D recombinants, may later emerge as significant stains in the pandemic. Full-length genome sequencing is an essential component of HIV 1 genetic analysis.

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