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A1 Signature pattern and phylogenetic analysis of full-length env genes in 20 hemophiliacs infected with Korean subclade of HIV-1 subtype B

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Twenty patients with hemophilia (HP) were diagnosed with HIV-1, one to two years after exposure to domestic clotting factor IX (DCF), in 1989–90. Previous analysis of pol and vif genes confirmed that HIV-1 transmission to 20 HPs occurred through infusion of DCF. In this study, we determined full-length env gene sequences (about 2,550 bp) in 21 HPs, three plasma donors whose plasma were used in DCF production, and 45 local controls. The env gene from frozen stored sera obtained 1–3 years after diagnosis as well as from samples collected years after infection, was amplified by RT-PCR, and subjected to direct sequencing. Phylogenetic analysis revealed that all sequences were subtype B, with 109 sequences from 64 patients (20 HPs, 3 serum donors, 41 local controls, LCs) belonging to the Korean subclade (KSB) and 13 sequences from 5 patients (1 HP infected outside Korea, 4 LCs) not in the KSB. Sequences of the env gene from donors O and P plus the 20 HPs comprised two subclusters within KSB. In addition, signature pattern analysis revealed signature nucleotides at 45 positions between the HPs and LCs ($P < 0.05$). Surprisingly, specific signature nucleotides positions were conserved 100% in clusters O and P only (at 4 and 1 positions, respectively) with none in LCs. Within both clusters, sequence identity was high. These results are consistent with our previous conclusion that these 20 HPs were infected with viruses in the DCF used for treatment. In addition, we found that there are 25 signature pattern residues in amino acids in env gene of KSB distinct from subtype B.

A2 HIV transmission networks among injection drug users in Pakistan

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Pakistan is currently facing a concentrated HIV epidemic among injection drug users (IDUs). Well-defined transmission networks, based on molecular epidemiology, have the potential to assist in the development of targeted screening and prevention strategies as well as identify hidden epidemic drivers. Here we present molecular transmission networks re-constructed from HIV-1 pol sequences collected from injection drug users located in major urban centres in Pakistan. Dried blood spots (DBS) were collected on Whatman 903 cards from IDUs in Karachi ($n = 300$), Hyderabad ($n = 300$), and Peshawar ($n = 257$). Nucleic acids were extracted using an easyMAG instrument. Protease and part of the reverse transcriptase genes were amplified and sequenced using an in-house HIV genotyping assay. Transmission networks were re-constructed using publicly available bioinformatics software. Most of the HIV pol sequences (75%) from 96 individuals formed connected nodes arranged in 7 clusters, ranging in size from 3 to 33 individuals. Clusters were mainly homogeneous, in which 87 inferred transmission events (90.6%) occurred within a particular city. A small number (9.4%) of transmission events occurred between cities. The highest number of inter-city transmission events (7.3%) occurred between Karachi and Hyderabad while only 2 (2.1%) occurred between Karachi and Peshawar. Transmission events were not observed between Hyderabad and Peshawar. The majority of sequences analyzed formed localized transmission networks partitioned according to city of collection, although some inter-city linkages are apparent. Reconstruction of transmission networks based on sequencing-based approaches has the potential to expand our understanding of the HIV epidemic currently taking place in Pakistan especially if used in combination with epidemiological data. Particular attention maybe warranted for Karachi since transmission linkages were observed with all the other cities included in this study.

A3 Genetic analysis and natural polymorphisms in HIV-1 gp41 isolates from Maputo, Mozambique

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Enfuvirtide is an HIV fusion inhibitor that prevents fusogenic conformation and inhibits viral entry into host cells. Resistance to Enfuvirtide is conferred by mutations occurring in the HR1 region of HIV gp41, involving residues 36–45. Mozambique, a sub-Saharan country with an HIV prevalence of 11.5%, provides