Predicted HIV-1 coreceptor usage among Kenya patients shows a high tendency for subtype D to be cxcr4 tropic

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Abstract

Background: CCR5 antagonists have clinically been approved for prevention or treatment of HIV/AIDS. Countries in Sub-Saharan Africa with the highest burden of HIV/AIDS are due to adopt these regimens. However, HIV-1 can also use CXC4R as a co-receptor. There is hence an urgent need to map out cellular tropism of a country’s circulating HIV strains to guide the impending use of CCR5 antagonists.

Objectives: To determine HIV-1 coreceptor usage among patients attending a comprehensive care centre in Nairobi, Kenya.

Methods: Blood samples were obtained from HIV infected patients attending the comprehensive care centre, Kenyatta National Hospital in years 2008 and 2009. The samples were separated into plasma and peripheral blood mononuclear cells (PBMCs). Proviral DNA was extracted from PBMCs and Polymerase Chain reaction (PCR) done to amplify the HIV env fragment spanning the C2-V3 region. The resultant fragment was directly sequenced on an automated sequencer (ABI, 3100). Co-receptor prediction of the env sequences was done using GenoZapheno (co-receptor), and phylogenetic relationships determined using CLUSTALW and Neighbor Joining method.

Results: A total of 67 samples (46 treatment experienced and 21 treatment naïve) were successfully amplified and sequenced. Forty nine (73%) sequences showed a prediction for R5 tropism while 18 (27%) were X4 tropic. Phylogenetic analysis showed that 46 (69%) were subtype A, 11 (16%) subtype C, and 10 (15%) subtype D. No statistical significant associations were observed between cell tropism and CD4+ status, patient gender, age, or treatment option. There was a tendency for more X4 tropic strains being in the treatment experienced group than the naïve group: Of 46 treatment experiencing participants, 14 (30%) harbour X4, compared with 4 (19%) of 21 of the treatment-naïve participants, the association is however not statistically significant (p = 0.31). However, a strong association was observed between subtype D and CXCR4 co-receptor usage (p = 0.015) with 6 (60%) of the 10 subtype D being X4 tropic and 4 (40%) R5 tropic.

Conclusion: HIV-1 R5 tropic strains were the most prevalent in the study population and HIV infected patients in Kenya may benefit from CCR5 antagonists. However, there is need for caution where subtype D infection is suspected or where antiretroviral salvage therapy is indicated.

Keywords: Co-receptor usage, HIV-1, Sub-type D