The presence of the Y181C mutation in HIV-1 group O strains is clade dependant

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BACKGROUND

Human Immunodeficiency Virus type 1 group O (for outlier, HIV-O) has emerged at about the same time as group M (for major, HIV-M), but remains endemic in Cameroon while HIV-M has became pandemic. The very localized diversification of HIV-O has resulted in a "comet-like" phylogenetic structure very different from the double star characterizing the HIV-M phylogeny. Two HIV-O classifications have been proposed on the basis of relatively few sequences, identifying five and three clades respectively, and both shown a disproportion with a majority of strains falling into clade I (Yamaguchi 2002) or A (Roques 2002) (fig.1).

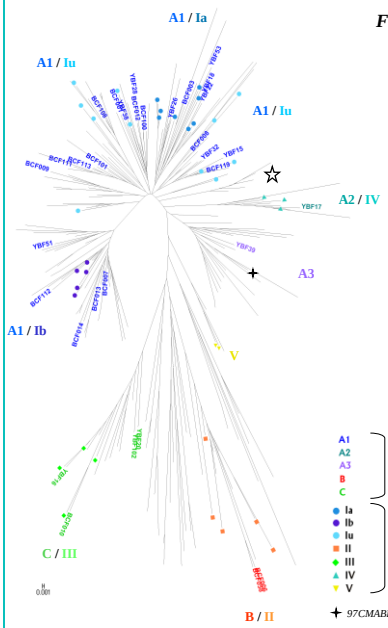

Fig.1: Phylogenetic analysis of 256 HIV-O partial gp41 sequences. *Sequences were aligned using MEGA.4 and manually edited when needed; 525 positions remained after removing those who could not be aligned unambiguously. Tree reconstruction was inferred using the Neighbor Joining method, and Tamura-Nei estimated distances using Γ-distributed rates along sites with parameter α=0,33.*

Most of the HIV-O strains are know to harbor a Y181C mutation in the Reverse Transcriptase (RT), leading to a possible natural resistance to the Non Nucleoside RT Inhibitors (NNRTIs); here we investigate the relationship between the presence of this mutation and the phylogenetic classification of HIV-O strains.

METHODS

136 samples from HIV-O infected NNRTI-naïve patients from France (n= 74) and Cameroon (n= 62) have been used for viral RNA extraction, amplification and sequencing in the protease and partial RT regions, phylogenetic analysis and Y181C mutation search.

RESULTS

Among the 136 strains, only 76 harbour a Y181C mutation, 93% of which belonging to cluster A, while Y181Y is found in 91% of the non-A strains (fig.2). One virus (0.8%) harbored a mixture Y181Y/C on sequential samples (**RBF165**).
Interestingly, the sub-clade A3, together with a cluster of sequences associated to A3 in this region (indicated with a star in both figures), but not in the gp41, show a 181Y residue for 24 sequences out of 26.
Note that the branching of the sub-clade A2 is different from the one observed in the gp41 region.

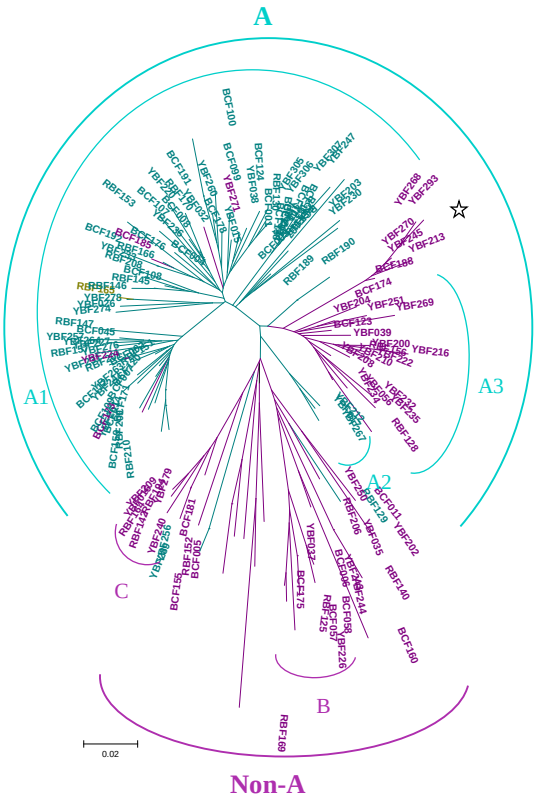

Fig.1: Phylogenetic analysis of 136 HIV-O partial pol sequences (987 positions encompassing the full protease and 230 codons of the RT) . *Sequences were aligned using MEGA.4. Tree reconstruction was inferred using the Neighbor Joining method and Tamura-Nei estimated distances using Γ-distributed rates along sites with parameter α=0,25.*

CONCLUSION

The wide diversity of group O viruses is still difficult to explore since it has resulted from a very localized evolution. As a consequence, there are only few and weakly defined clusters, and many strains remain unclassified, but some clusters (as AI/Ib and A3/U) become significant with the contribution of new sequences.
Despite the dichotomy between a major "clade" A and the other sequences, we show that A3 can share some characteristics with non-A sequences, and interestingly, 97CMABB497, the only sequence belonging to this cluster which appeared in Yamaguchi's analysis and remained unclassified, could be of recombinant origin (Yamaguchi 2003). Moreover, the cluster A2 and another unclassified cluster from the major clade show evidences of recombination.
Further investigations, using more tools and larger sets of sequences in different regions of the genome, are needed to better understand the evolution of HIV-O and possibly define a relevant nomenclature.