



# Next Generation Sequencing Analysis of HIV-1 Group O Reverse Transcriptase Residue 181C Prevalence and Evolution over Time, With or Without Antiretroviral Selection Pressure

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# Next Generation Sequencing Analysis of HIV-1 Group O Reverse Transcriptase Residue 181C Prevalence and Evolution over Time, With or Without Antiretroviral Selection Pressure

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## BACKGROUND

HIV-1 group O viruses are endemic in Cameroon and found sporadically in other countries. Their genetic divergence from pandemic HIV-1/M causes polymorphisms on residues associated to HIV-1/M antiretroviral resistance.

### HIV-1 group M:



Non-Nucleotide Reverse Transcriptase Inhibitors (NNRTI) resistance mutation Y181C can be selected in HIV-1/M but naturally present in HIV-1/O, and associated to the recently emerged HIV-1/O-H subgroup<sup>1</sup>. A previous study suggested that residue 181C could confer a better replicative fitness to HIV-1/O *in vitro* and that signature residues were associated to 181Y-like or 181C-like lineages<sup>2</sup>.

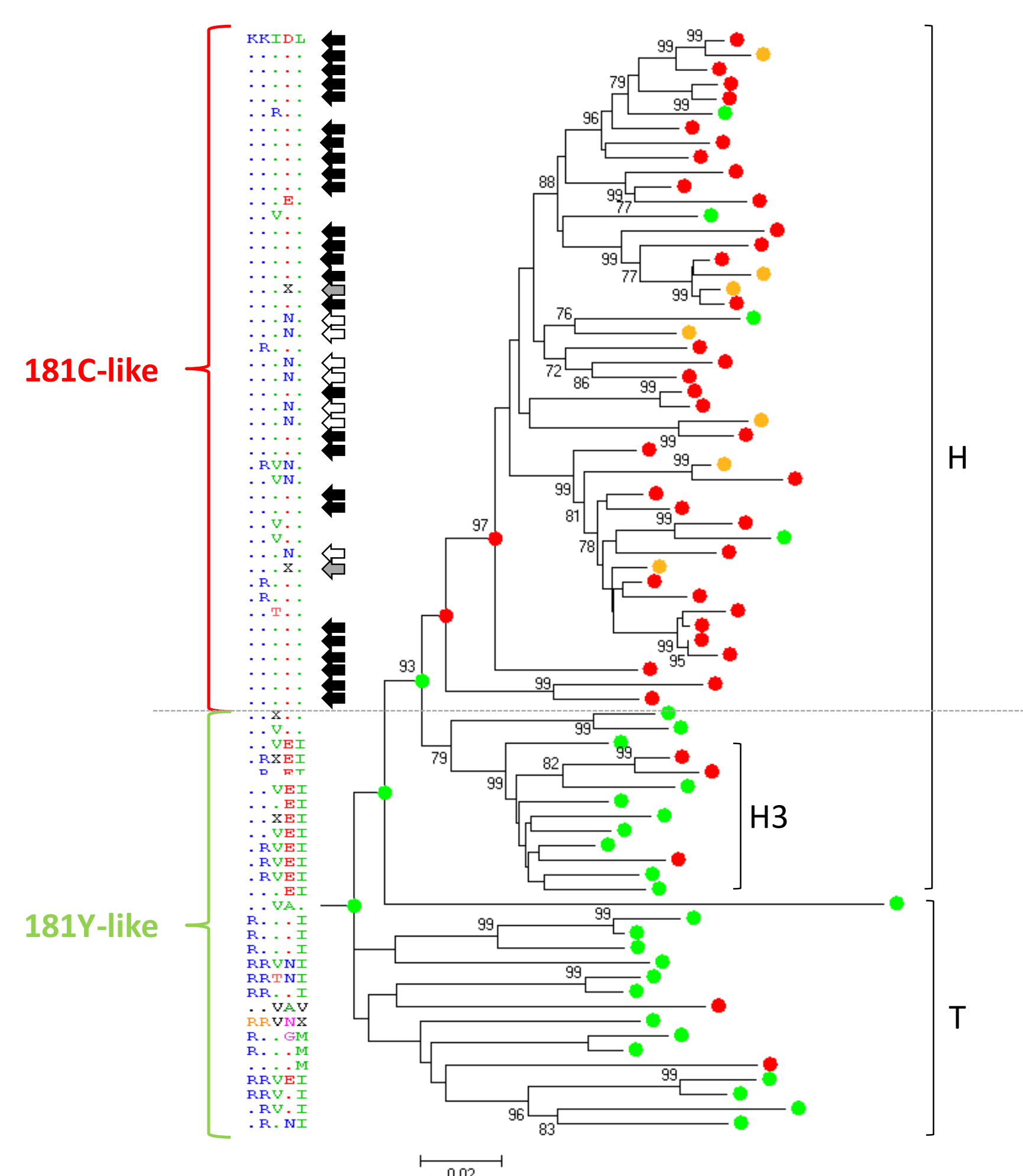
Here we aimed at exploring these hypotheses using *in vivo* samples and to investigate evolution of group O RT residue 181 under selection pressure due to NNRTI based treatment or not.

## METHODS

We used Next Generation Sequencing to study residue 181 distribution and associated signature residue polymorphisms in 75 NNRTI-naïve HIV-1/O patients (1). Evolution of residue 181 over time – under selection pressure due to NNRTI based treatment or not – was investigated by Sanger and confirmed by NGS for some samples in 8 patients (2). We compared the viral loads from 59 untreated patients depending on residue 181 (3).

## RESULTS (1)

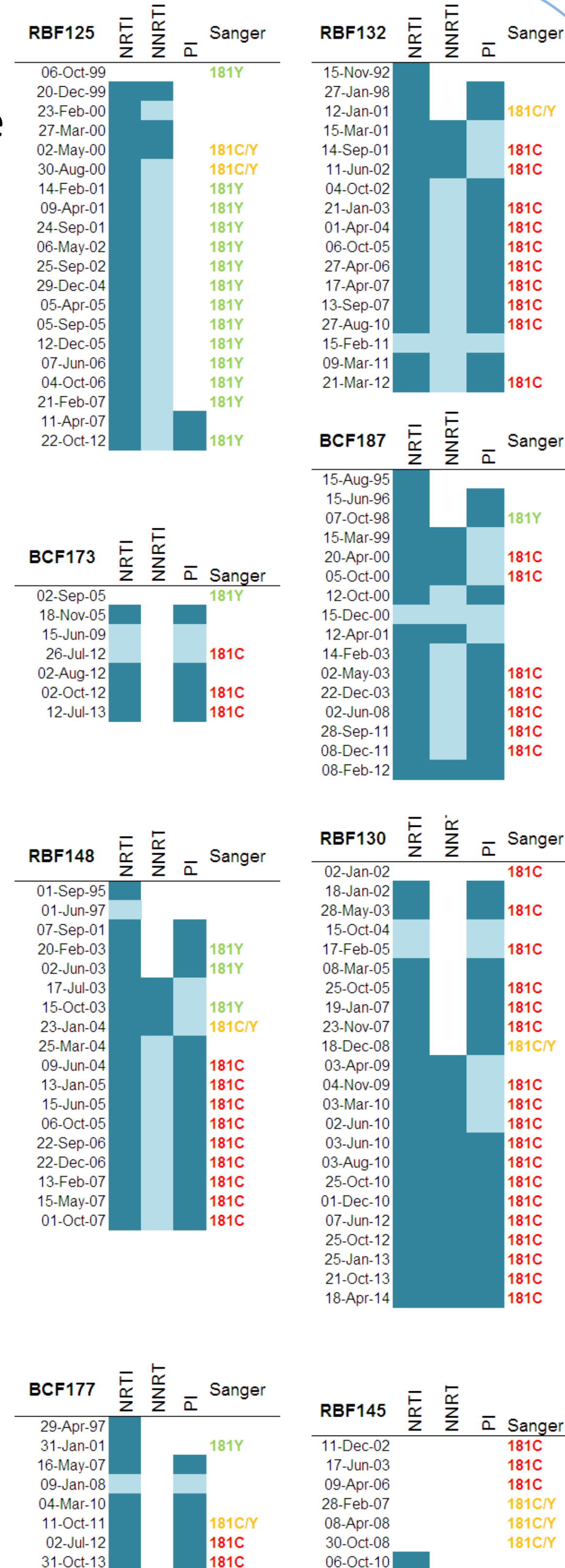
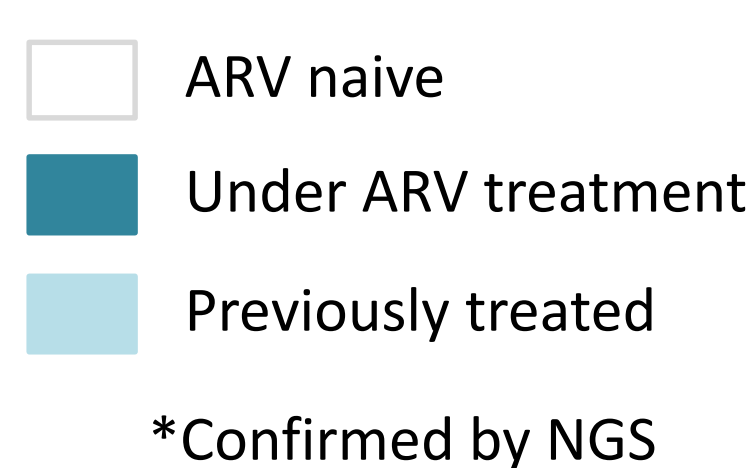
Residue 181C (red) was found in 40/75 NNRTI naïve patients. Its association with HIV-1/O-H was confirmed ( $p < 0.001$ ). A 181C/Y mixture (orange) was found in 7 unlinked individuals.



Residues at signature positions were diverse in 181Y viruses (green) but a 28K-103K-142I-174D-178L pattern was highly conserved in 181C viruses (black arrows).

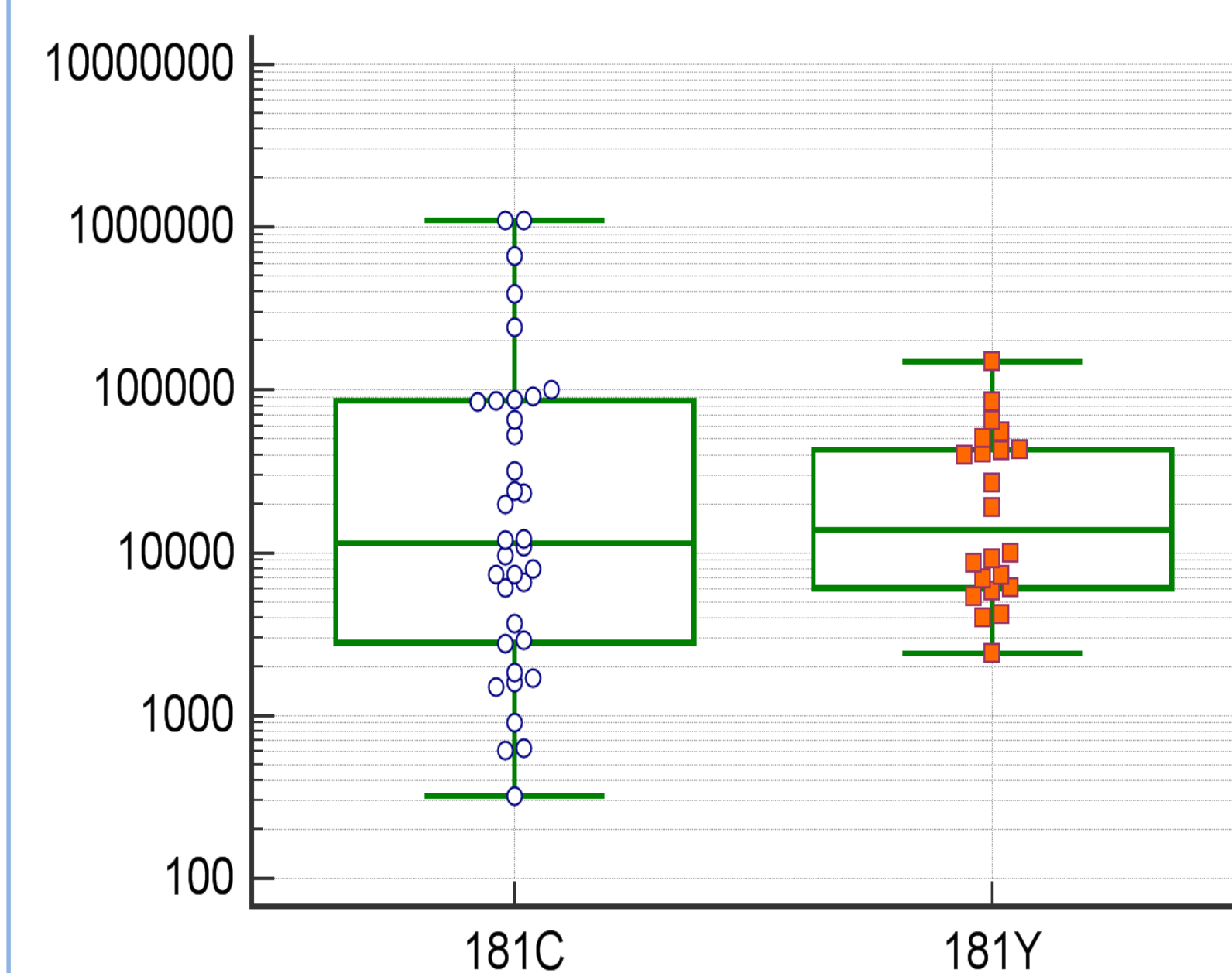
## RESULTS (2)

Evolution of residue 181 was similar to what observed under NNRTI in HIV-1/M for one 181Y HIV-1/O-T virus (RBF125). Three HIV-1/O-H viruses selected 181C due to NNRTIs, but conserved it several years after NNRTI interruption (RBF132, BCF187, RBF148). Four HIV-1/O-H viruses evolved without NNRTIs (C/Y => C, n=2, C => C/Y, n=2).



## RESULTS (3)

The viral load range in untreated patients infected by 181C viruses (min: 2.5log cp/ml ; max: 6.0log cp/ml; N=37) was larger than that of 181Y virus infected patients (min: 3.4log ; max: 5.2log; N=22).



The mean viral load was higher in the 181C group (5.1log, median: 4.1log) than in the 181Y group (4.5log, median: 4.2log), but not significantly according to Student t test ( $p=0.14$ ).

## CONCLUSIONS

Mutation 181C presence and evolution in HIV-1/O is **linked to the virus genetic background**.

It is associated to the emergent HIV-1/O-H subgroup where it can be **naturally present, or conserved after NNRTI selection**, possibly due to a favourable pattern (28K-103K-142I-174D-178L) on **associated signature residues**.

However, **no replicative advantage** is observed for 181C viruses *in vivo*.