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DUAL HIV-1/M+O INFECTIONS AND HIV-1/MO RECOMBINANTS

IN FRANCE FROM 2004 TO 2014







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BACKGROUND

HIV-1 exhibits a high genetic diversity. It is currently divided into 4 groups: M, N, O and P as shown on figure 1^[1]. Recombination is a crucial mechanism of HIV evolution, and HIV-M recombinants now account for more than 20% of HIV-1 infections^[2]. HIV-M and HIV-O cocirculation in Cameroon led in few patients to dual infections and to subsequent generation of MO recombinants (MOrecs). The first dual M+O infections were described in Benin in 1995^[3] and 3 MOrecs were identified in Cameroon in 1999^[4,5] and 2004^[6]. Due to historical links with Western Central Africa, sporadic cases of superinfection/dual infections^[7,8] and MO recombinant infection^[9] were also described in France.

The aim of this study was to determine the circulation level of dual M+O Infections and associated MO recombinant forms in the last decade in France.

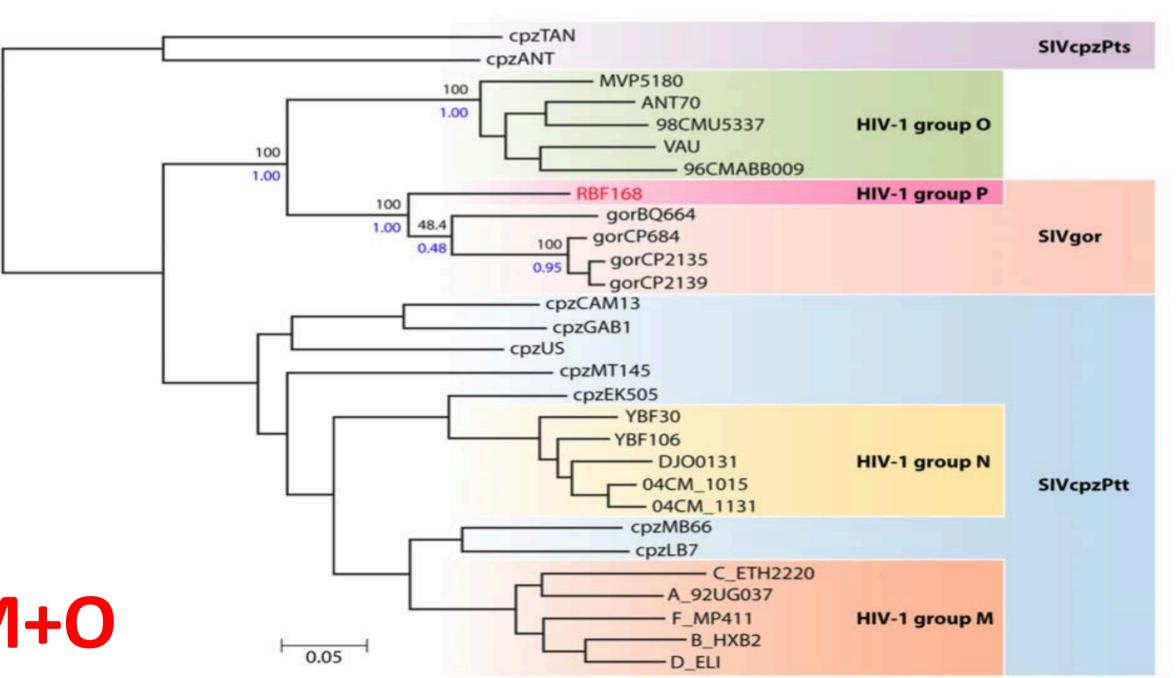


Figure 1. Genetic diversity of HIV-1¹

RESULTS

The presence of both M and O genomes were detected in 10/141 (7%) HIV-O infected patients.

The analysis of these cases allowed us to identify different situations:

- 2 M+O dual infections in 2 patients (RBF140 in 2004 and RBF216 in 2009),
- 3 MO recombinants associated:
 - with the HIV-O parental strain in 2 epidemiologically linked patients (BCF174, 2005 and BCF212, 2006)
 - with both the M and O parental strains in 1 patient (RBF235, 2007)
- 6 MO recombinants without parental strains:

- RBF208 (2008), RBF221 (2 recombinants in the same patient, 2010), RBF222, (2010), RBF237 (2013), BCF204 (2013)

For each of these MO recombinants, whole genome or partial sequences were analyzed. All the MO recombinant genetic patterns were different with breakpoints in LTR (1 in 8), p17^{GAG} (1 in 8), RT (3 in 8), INT (2 in 8), gp41 (1 in 8) and/or accessory genes (9 in 8) as shown in the figures 2 and 3.

The 2 viruses found in the same patient RBF221 exhibited multiple breakpoints in the accessory genes (at least 2 and 5 respectively).

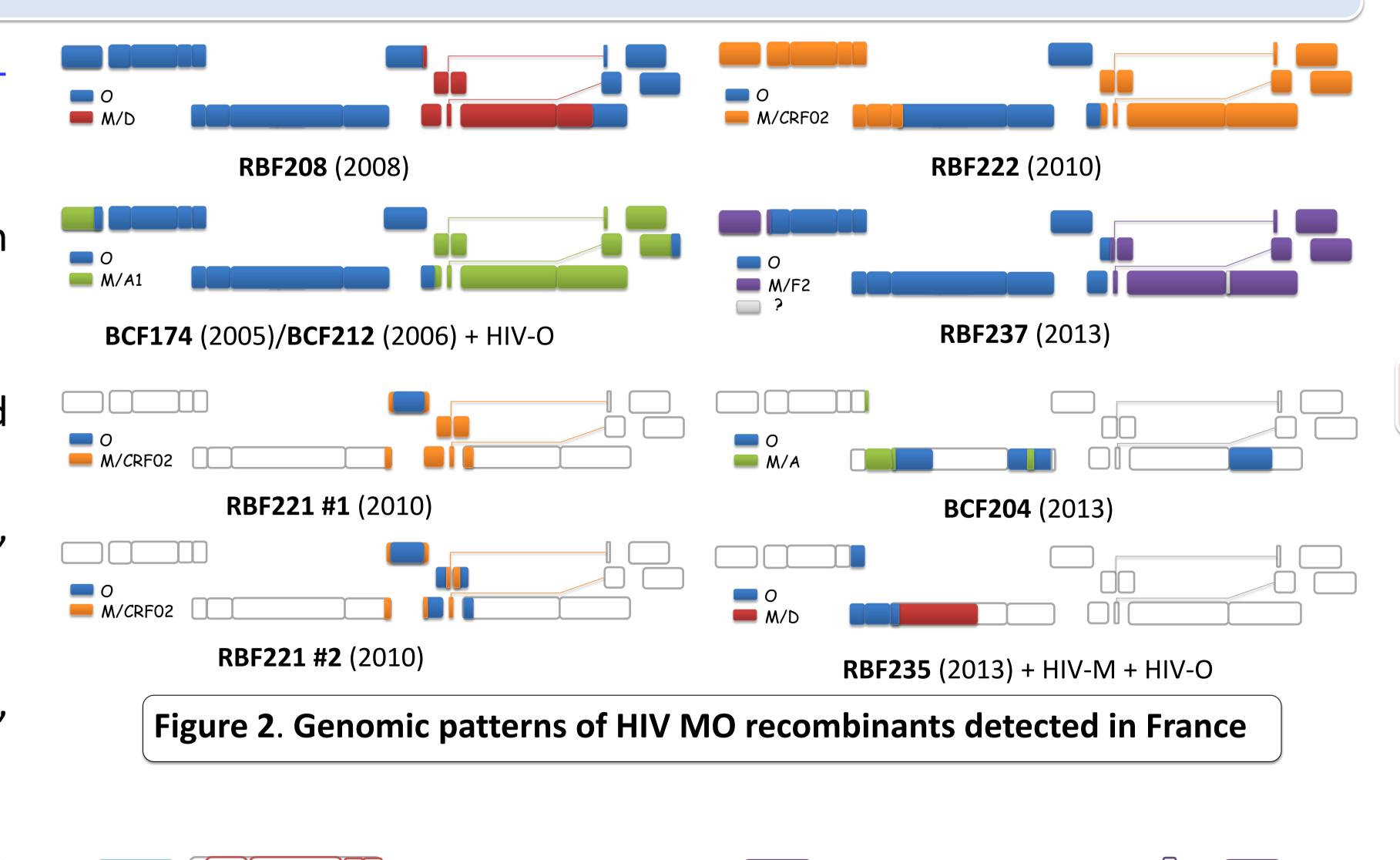
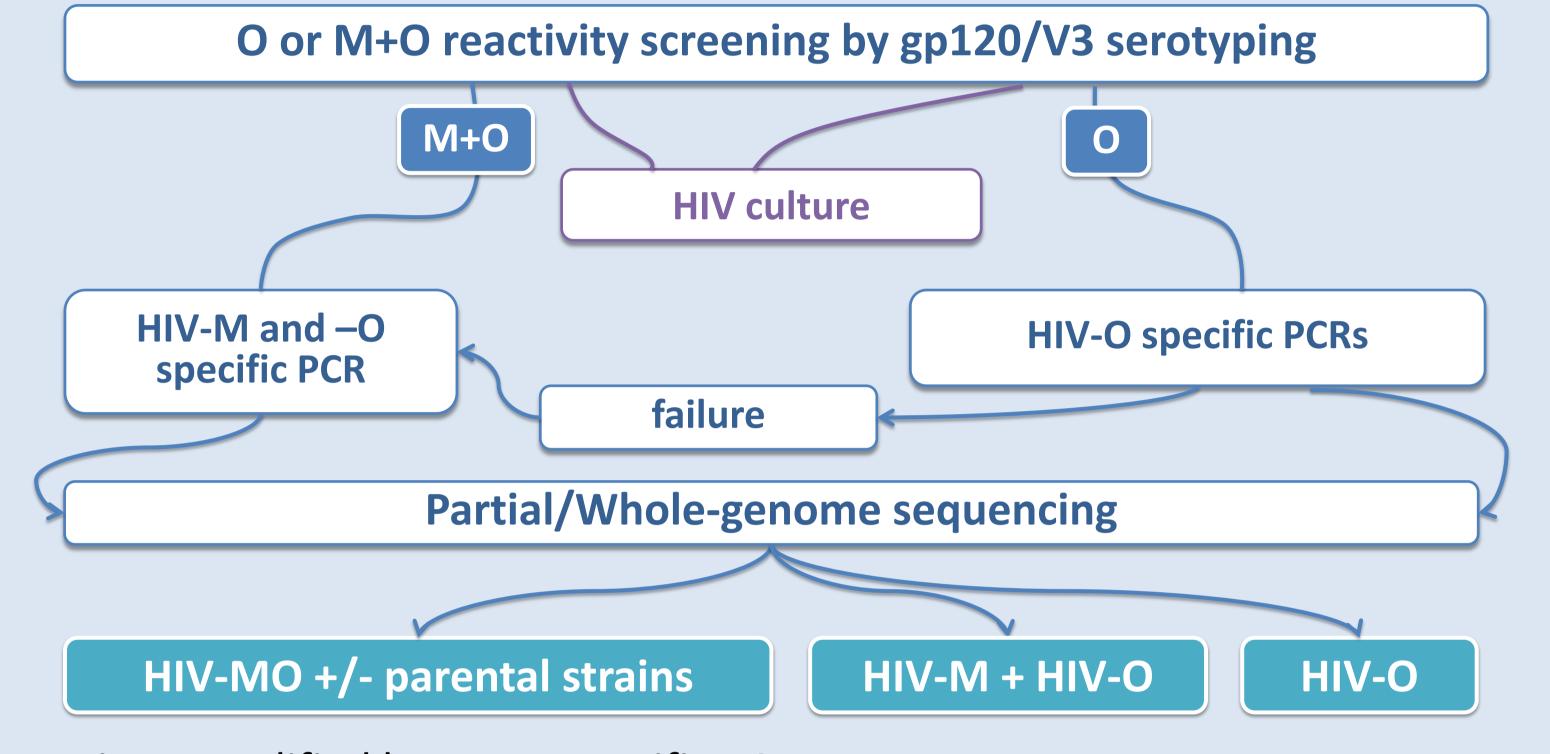


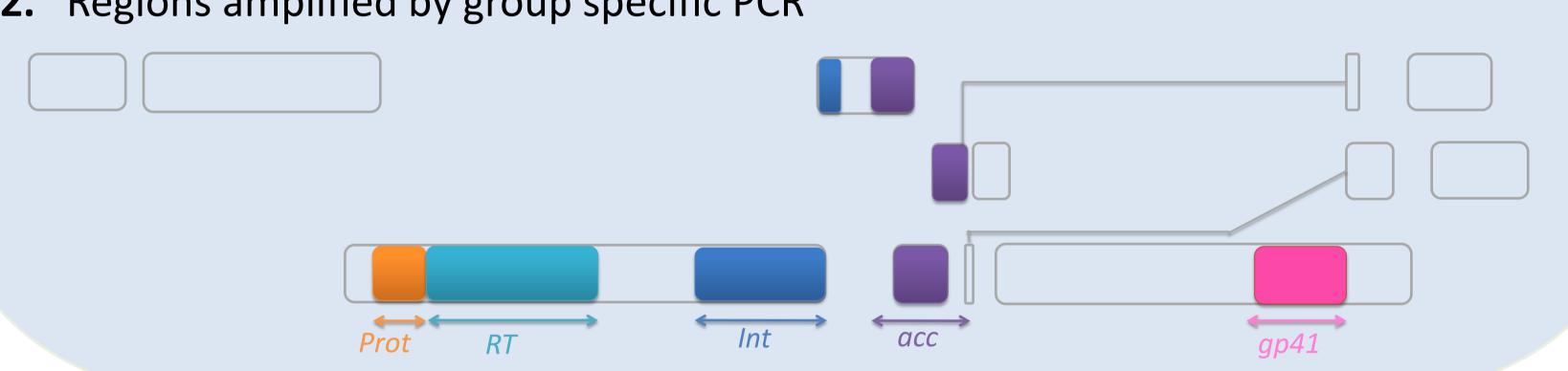
Figure 3. Breakpoints found in vivo in MOrecs in France (blue arrows) and in previous publications (orange arrows)

METHODS

1. The presence of both M and O genomes were looked for HIV-M+O / HIV-MO screening in 141 HIV-O patient samples collected from 2004 to 2014 by the RESO/French HIV-National Reference Centre



2. Regions amplified by group specific PCR



Conclusions

Although all described in Cameroonian native patients, we show 11 HIV-M+O dual infections and/or HIV-MO recombinant infections in the past decade in France, highlighting these phenomenons are not so rare. Moreover, the presence of MO recombinants circulating without the presence of parental O or M strains, and in epidemiologically linked patients demonstrate they are fit enough to be transmitted and spread. Finally, as HIV-O are naturally resistant to NNRTIs, the transmission of dual HIV-M+O infections or MO recombinants carrying HIV-O genomic fragments underline the importance of searching for these forms, evaluating their spread dynamics and following the possible emergence of a CRF MO.

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