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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 co-circulation 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.

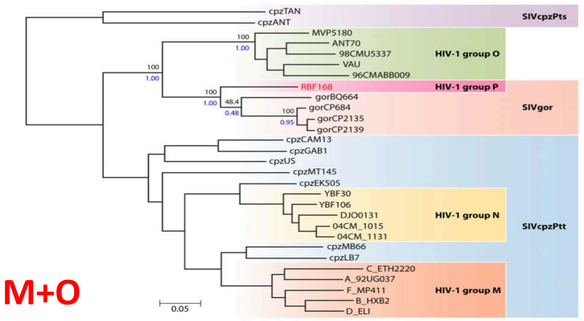


Figure 1. Genetic diversity of HIV-1[1]

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).

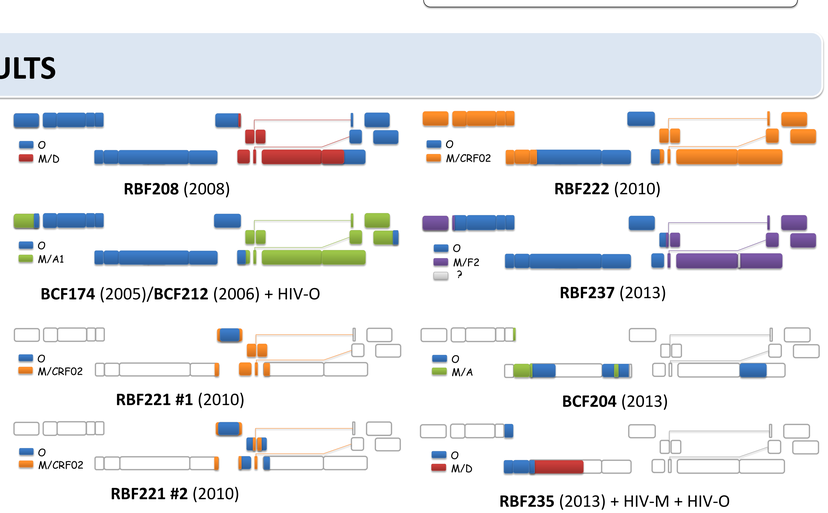


Figure 2. Genomic patterns of HIV MO recombinants detected in France

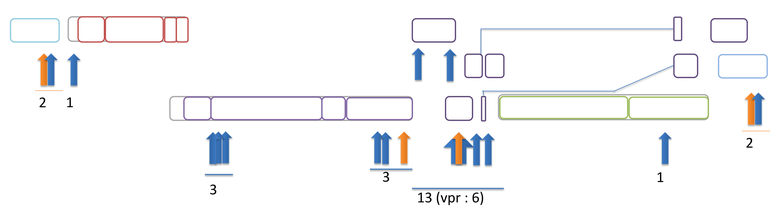
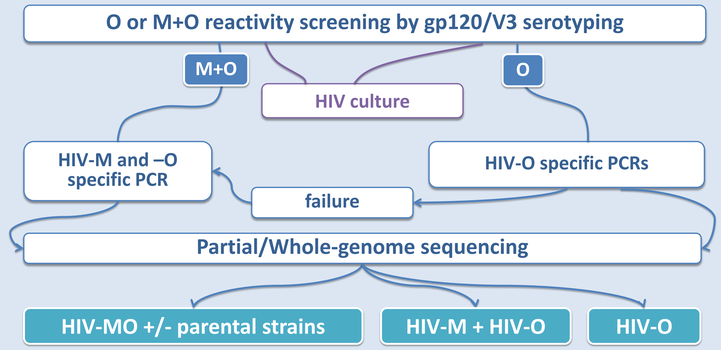


Figure 3. Breakpoints found *in vivo* in MOrecs in France (blue arrows) and in previous publications (orange arrows)

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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