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HIV-1/M+O INTERGROUP DUAL INFECTIONS AND ASSOCIATED HIV-MO RECOMBINANTS IN FRANCE FROM 2004 TO 2014

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BACKGROUND

HIV-1 exhibit 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 the 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, dual infections^[7,8] and MO recombinant infections^[9] have also been described in France.

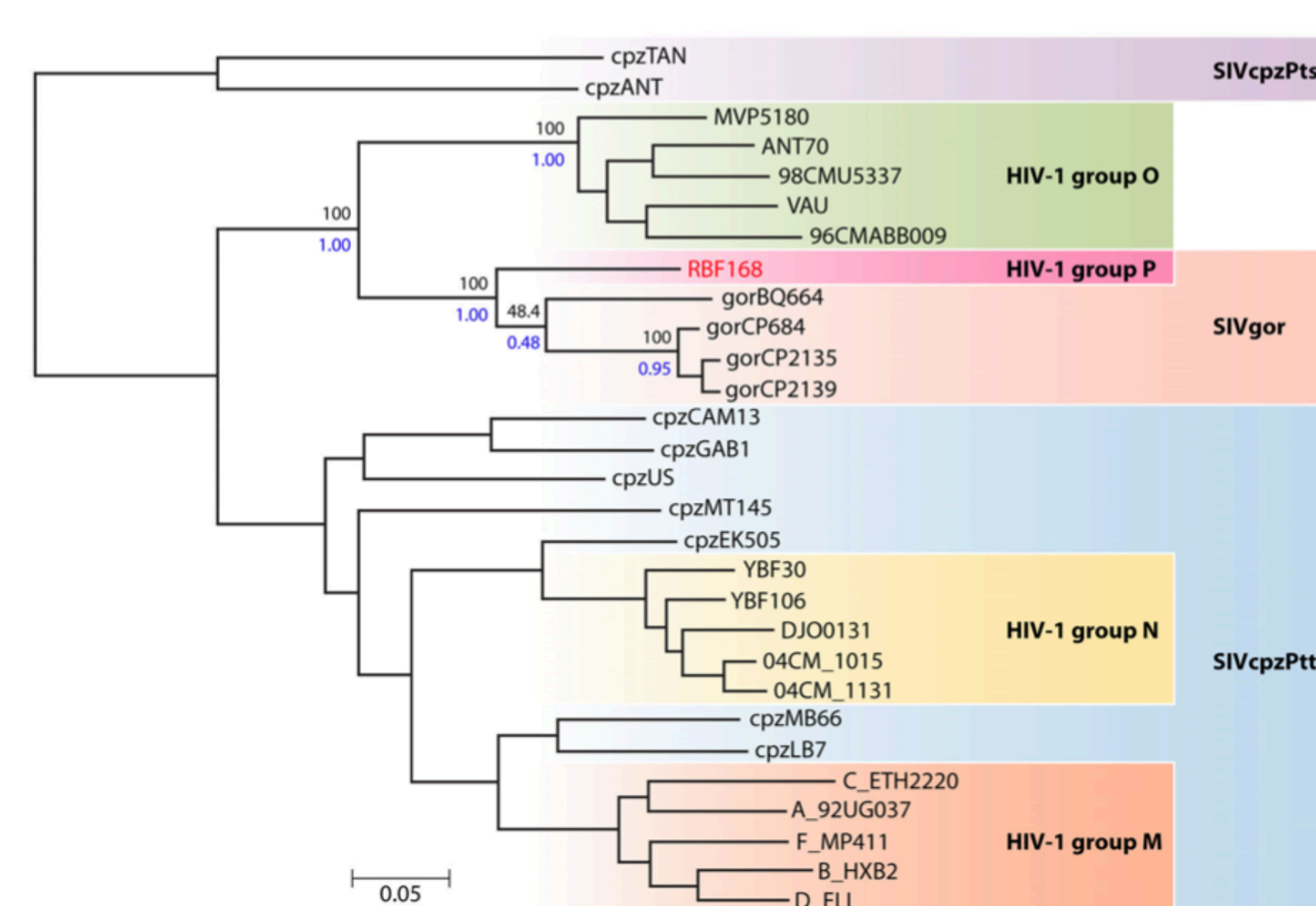


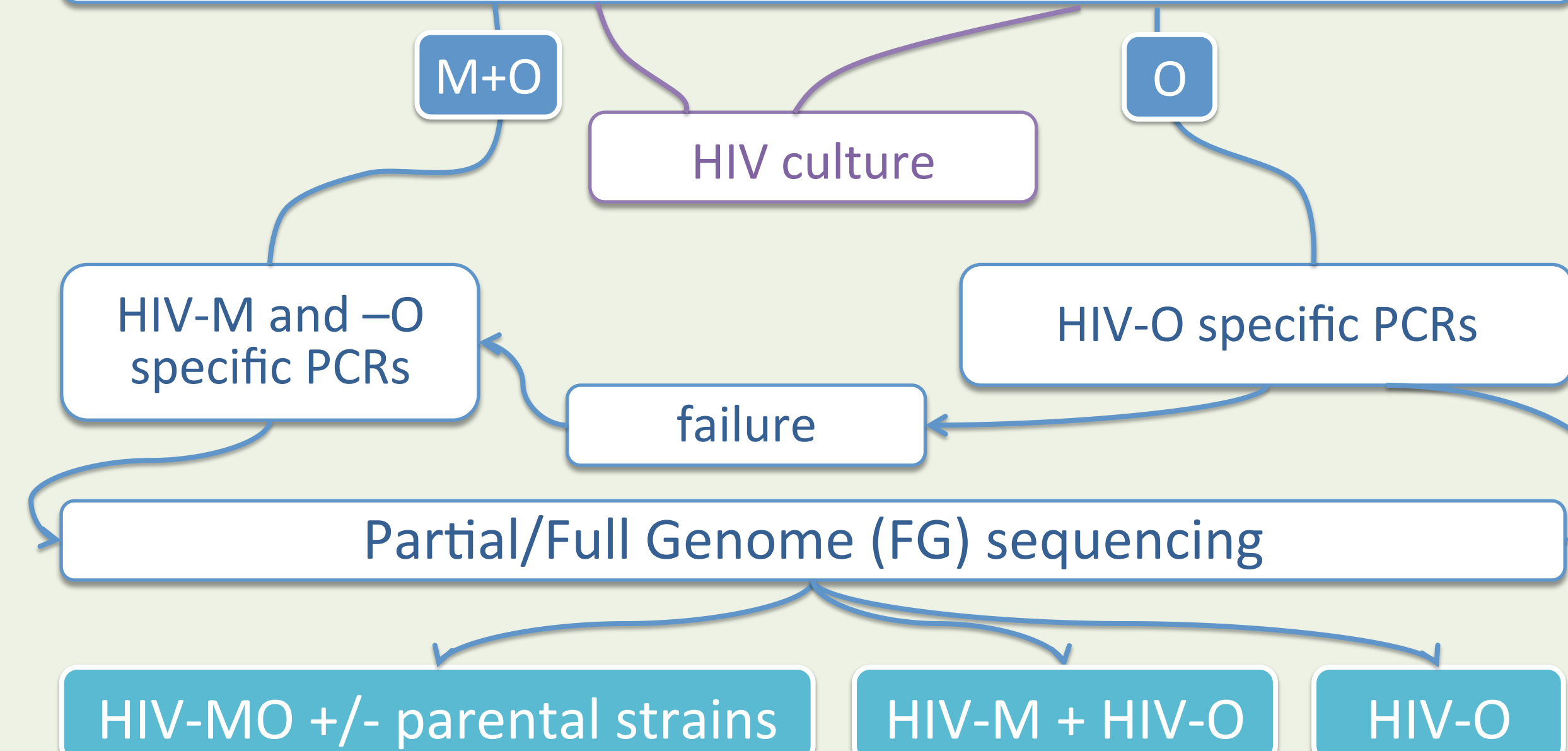
Figure 1. Genomic diversity of HIV-1¹

In this study, we aimed to detect these forms among patients diagnosed in France with an HIV-O infection, and characterising the MOrecs genomic patterns found *in vivo*.

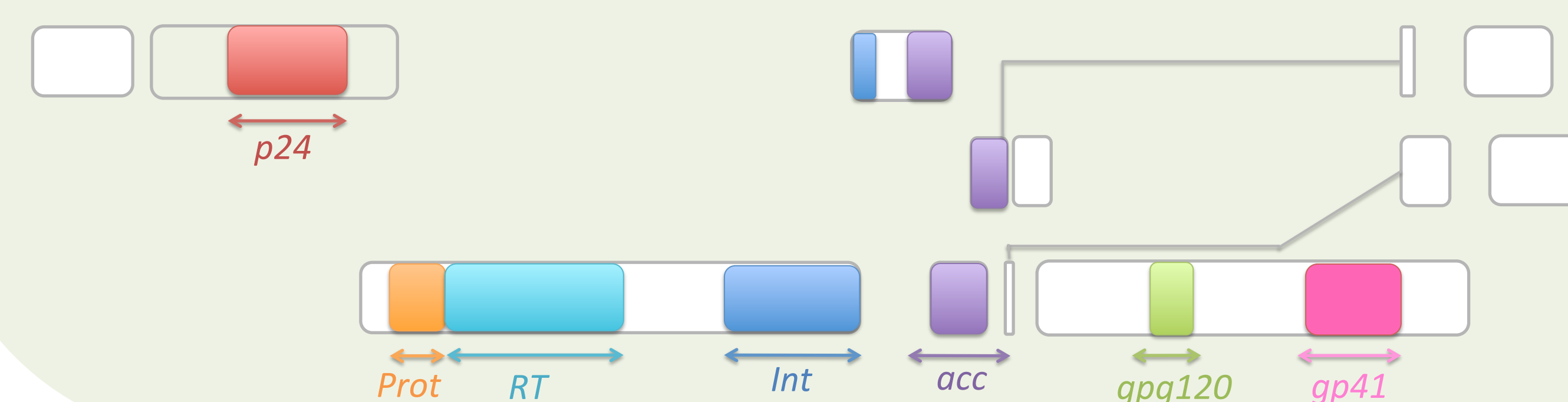
METHODS

1. 141 HIV-O patients samples (2004-2014): RESO/HIV-National Reference Centre (NRC)---> HIV-M+O / HIV-MO screening

M+O dual reactivity screening by gp120/V3 serotyping



2. Regions amplified by group specific PCRs used for genotypic resistance detection or as part of the NRC activities.



RESULTS

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

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

- **2 M+O dual infections** in 2 patients (in 2004 and 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 (**BCF204**, 2013)
- **6 MO recombinants without parental strains** :
 - **RBF208** (2008), **RBF222**, (2010), **RBF234** (2013), **RBF221** (2 recombinants in the same patient, 2010), **RBF235** (2013).

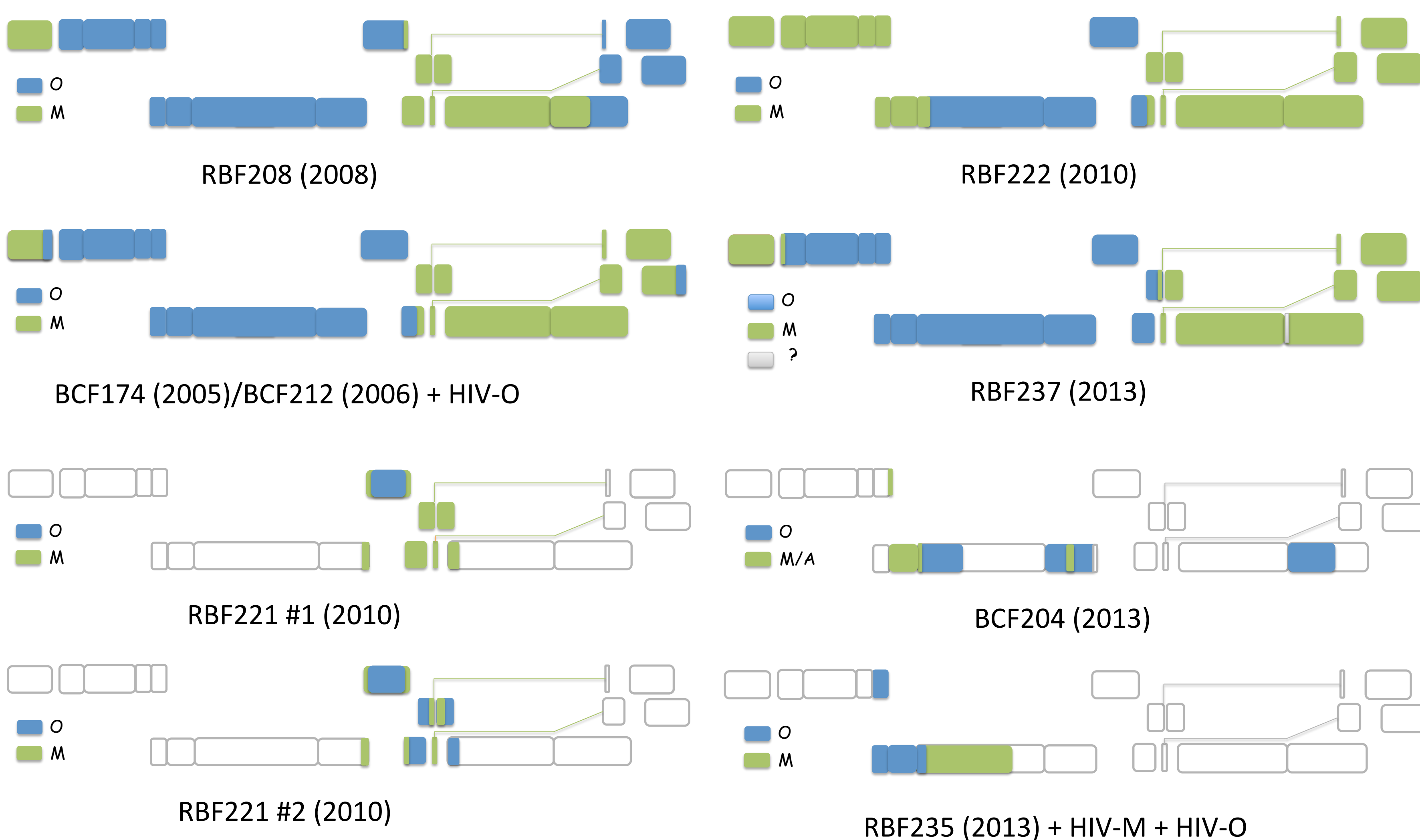


Figure 2. Genomic patterns of HIV MO recombinants detected in France

For each of these MO recombinants, whole genome or partial sequences were analysed. All the MO recombinant genetic patterns were different with breakpoints in LTR (1/8), $p17^{GAG}$ (1/8), RT (3/8), INT (2/8), gp41 (1/8) and/or accessory genes (6/8) as shown in the **figure 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).

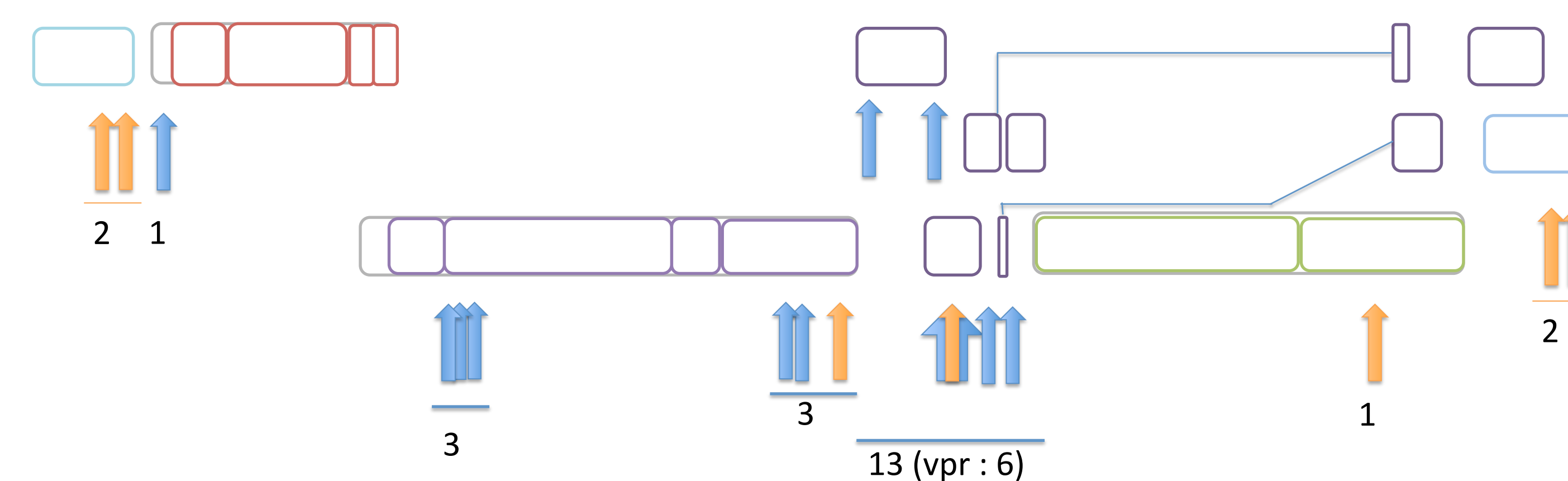


Figure 3. Breakpoints found *in vivo* in MOrecs in France (blue arrows) and in previous publications (orange arrows)

Conclusion

Although all described in Cameroonian native patients, we showed HIV-M+O dual infections and MOrecs circulate in France. Moreover, the presence of MO recombinants circulating alone 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 HIV-M+O dual infections or MOrecs carrying HIV-O genomic fragments underline the importance of searching for these forms, evaluate their spread dynamics and follow the possible emergence of a CRF_{MO}.

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