



## First Evidence of a HIV-1 M/O Recombinant Form Circulating Outside Cameroon

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## INTRODUCTION:

HIV-O infection is endemic in Cameroon. Among these patients HIV-O positive (= 1% of all HIV infections), seroprevalence studies showed at least 10% of HIV-M/HIV-O dual infections, but only three O/M recombinant forms have been previously described [1, 2, 3].

In France, 119 patients have been yet identified with HIV-O infection, most of them originating from Cameroon. The suspicion of HIV-O infection often comes on the occasion of diagnosis difficulties or virological-clinical discordances due to their high genetic divergence compared to HIV-M, which can lead to poor or total lack of detection by certain commercial tests.

## PATIENTS AND METHODS:

A 25years old Cameroonian woman (RBF209) living in France since 2000 had consulted at the University Hospital of Reims (eastern France) in May 2008. Her biological and virological analyses indicated (*tab.1*):

-CD4 = 6/mm<sup>3</sup>

- viral load = undetectable (Roche Cobas Taqman)

- viral load =  $6.10^4$  cop/ml (Abbott Realtime)

Complementary analyses were performed using :

- in-house HIV-O specific viral loads, targeting the LTR and integrase regions

-serotyping assay using peptides that mimic the Immuno-Dominant Region (IDR) of the gp41 and the V3 loop of the gp120 specific to HIV-1 groups M, N and O and HIV-2

- HIV-O or M group-specific PCR in the Protease, Reverse Transcriptase (RT), Integrase and Gp41 regions

- near full-length genome characterization from viral RNA and intracellular DNA, using non specific XL-RT-PCR and XL-PCR, and sequencing with a set of 37 primers.

## RESULTS:

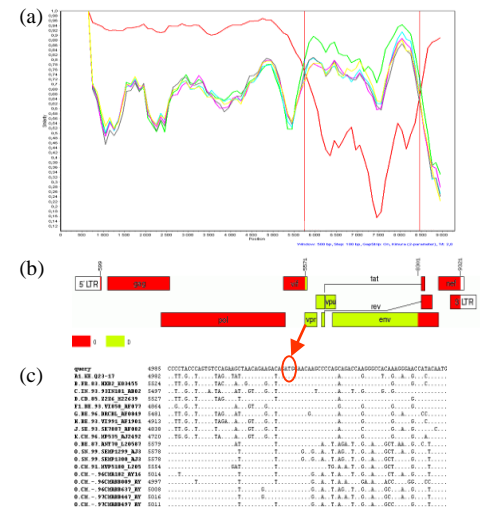
The viral loads results were firstly in favour of a group O infection. The HIV-M specific Roche Cobas Taqman test was undetectable while the HIV-O specific methods were positive as the non specific Abbott M2000 (*tab.1*). However, serotyping clearly indicated a specific group M reactivity (*fig.1*).

Group specific amplifications were positive only for HIV-O in the *pol* gene, and surprisingly no group-specific amplification was positive in the gp41 region (*tab. I*).

The near full length sequencing of the circulating viral RNA revealed a O-M-O recombinant form (*fig.2*) with a breakpoint in the gp41 region, explaining the negative results with group-specific primers. Another breakpoint was located on the first codon of *vpr*, where two of the three previously described M/O recombinants already shown a group switch.

Phylogenetic analyses indicated that RBF209 was not linked to the other M/O recombinants (*fig.3*).

The absence of HIV-O specific antibodies (*fig. 1*) together with the negativity of group M specific PCR in the *pol* gene and no amplification of M or O in the *gp41*, suggest that this young patient does not carry the parental HIV-O and HIV-M strains.



**Figure 2: Characterization of the near full length O-M-O recombinant form.** (a) Similarity plot indicating a HIV-O / HIV-M subtype D / HIV-O structure; (b) mapping the breakpoints on HIV-1 genome; (c) evidence of O/M recombination on the first codon of *vpr*

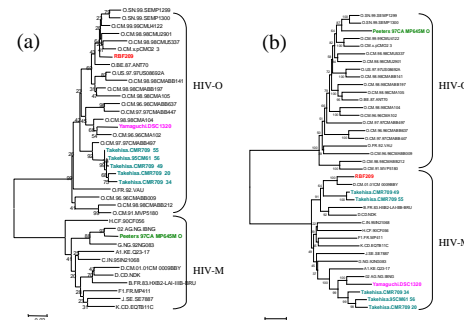
### CONCLUSION:

This fourth intergroup M/O recombinant form is the first described **outside Cameroon**.

Unlike the previously described cases which emerged during a co-infection, this could be the first **direct transmission** by a M/O recombinant form ever described, emphasizing the dynamic and a possible spread of such strains.

This kind of genome structure has consequences for the **follow up and treatment** of the patient, as there are HIV-O related mutations in the *pol*-encoding protease, RT and integrase, but targets of the entry inhibitors are HIV-M.

With three intergroup recombinants switching in the *vpr* gene and the fourth at the end of the integrase, the hypothesis of a **hotspot of intergroup recombination** in *vpr* or around the accessory genes region has to be explored.



**Figure 3:** Phylogenetic analysis of the integrase region (a) and the *vpr* to *gp120* region (b) of the RBF209 isolate together with the three previously described M/O recombinant forms. Method: Neighbor-Joining (1000 bootstraps tests), Distances Calculation: Kimura-2-Parameters model

**REFERENCES:**

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