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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/mm³
- viral load = undetectable (Roche Cobas Taqman)
- viral load = 6.10⁴ 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.

		target region								
		LTR	gag	protease	RT	Integrase	gp120 V3	gp41		
Viral Loads (log)	Roche Taqman									
	Abbott M2000									
	In house LTR	4.1					4.8			
	In house HIVO						5.0			
Serotyping	PLA									
Group-Specific Amplification	VHMO									
	VHMM									

Table 1: Viral loads, serotyping and group-specific amplifications results. Group O specific results are indicated in red, group M specific in green, and non specific in blue.

Figure 1: Optical densities observed using IDR peptides (a) or V3 peptides (b) of various HIV types and groups

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 (*fig1*).

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.1*).

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 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

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.

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