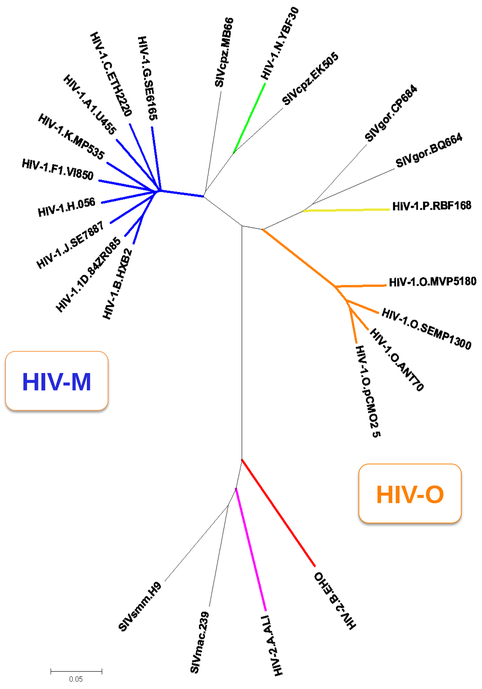
The Two Phases of HIV-1 Group O Diversification

Marie Leoz[1,2*], Felix Feyertag[3], Anfumbom Kfutwah[4], Philippe Mauclère[5], Guillaume Lachenal[6], Florence Damond[7], Véronique Lemée[8], François Simon[9], David L Robertson[3], Jean-Christophe Plantier[1,2, 8]

[1]Laboratoire de Virologie, CHU Charles Nicolle, Rouen, France; [2]EA 2656 GRAM, Université de Rouen, Rouen, France; [3]Computational and Evolutionary Biology, Faculty of Life Sciences, University of Manchester, Manchester, UK; [4]Service de Virologie, Centre Pasteur du Cameroun, Yaoundé, Cameroun; [5]Direction Interarmées du Service de Santé, Nouméa, Nouvelle Calédonie; [6]Laboratoire SPHERE, UMR 7219, Université Paris Diderot & Institut Universitaire de France, Paris, France; [7]Service de Virologie, APHP CHU Bichat Claude Bernard, Paris, France; [8]Laboratoire associé au Centre National de Référence du VIH, CHU Charles Nicolle, Rouen, France; [9]Service de Virologie, APHP CHU Saint Louis, Paris, France

BACKGROUND



Each group represents an independent **cross-species transmission** of SIV (Simian Immunodeficiency Viruses) to humans.

Group M is **pandemic** : >34,000,000 infections worldwide;

Groups N and P **very rare**: <20 infections linked to Cameroon;

Group O is **endemic in Cameroon**: ~ 10,000 to 30,000 infections.

Group O MRCA (Most Recent Common Ancestor) has been estimated to be **as ancient as group M** based on few sequences available. But group O genetic diversity and evolution remains poorly characterized.

OBJECTIVE

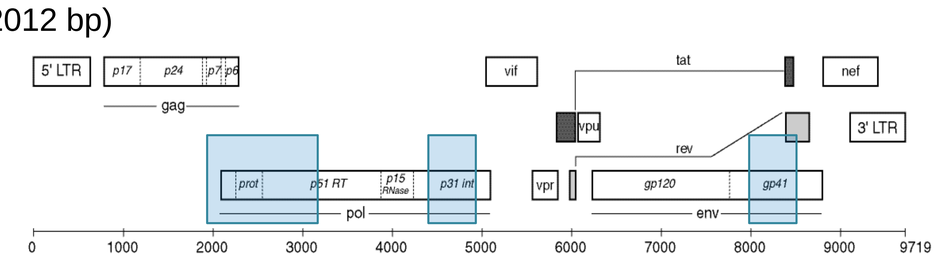
To explore HIV-1 group O genetic diversity and evolution through the largest series of HIV-O sequences, from Cameroon (samples used for HIV-O diagnosis and follow-up in the Centre Pasteur du Cameroun), France (RES-O surveillance network of the HIV National Reference Center) and Gabon**.**

METHODS

190 patients: 102 from France + 87 from Cameroon + 1 from Gabon

Sampling times ranging from **1987 to 2012** (25 years)

Three genome regions amplified, sequenced and concatenated (2012 bp)



Maximum Likelihood Tree Inference

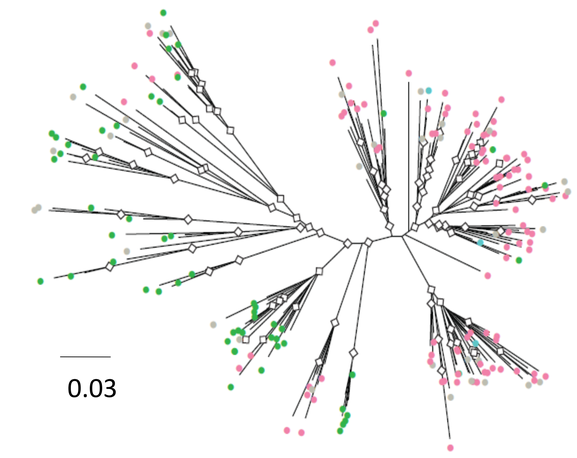
Distribution of Natural Y181C Resistance Mutation

Evoutionary Analyses (tMRCA and Bayesian Skyline)

RESULTS

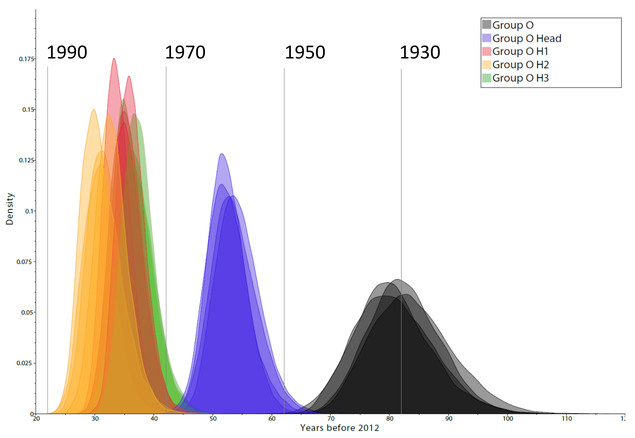
HIV-1 group O ML tree topology is atypical, with a **predominant clade** emerging from and broad and genetically diverse base population.

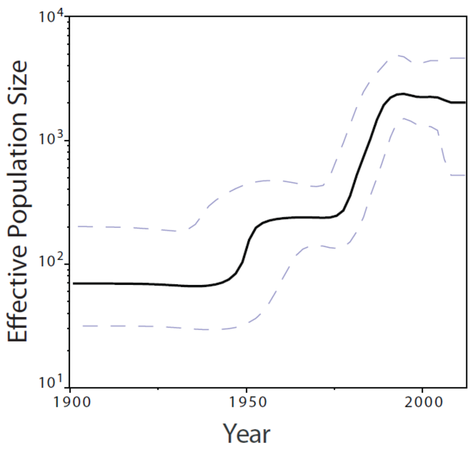
The **natural presence** of the Y181C mutation, conferring **resistance to NNRTIs**, is significantly associated to the **emergent clade** ($p<0.01$).



Sequence from NNRTI-naive patient with 181C residue
Sequence from NNRTI-naive patient with 181Y residue
Sequence from NNRTI-treated patient or no data on ARV treatment

HIV-1 group O MRCA is estimated **around 1930** (black curves). The **predominant clade** is more recent, with a MRCA estimate around 1960 (blue curves). Several subclusters emerged even more recently, in the 1980's (yellow, green and red curves).





HIV-1 group O diversification went through **two exponential phases,** in the 1950's and in the 1980's.

The now **predominant population** arose during the second phase, from an **ancestral level** of genetic diversity which had developed during the first diversification wave.

According to the historical context in Cameroon, the 1st wave might have been favored by **iatrogenic** routes of transmission in the 1950's, while the second would have benefited from the development of **urbanization**.

CONCLUSIONS

HIV-1 groups M and O share a **similar age** but group O has remained largely **confined to Cameroon**.

Group O local diversification resulted in a **broad genetic diversity** that cannot be compared to group M subtypes. However, **two subgroups** can be observed, corresponding to **two successive phases of diversification**.

The viral properties of the two subgroups need to be investigated, in order to better understand why the **most recent population** to emerge has now become **predominant**.

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