EVOLUTION OF CLUSTERS TRANSMISSION PATTERNS IN FRANCE DURING THE LAST DECADE

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CROI Conference on Retroviruses and Opportunistic Infections

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BACKGROUND

- The recent transmission clusters (RTCs), that can be identified through phylogenetic approaches, allow to describe the most active HIV transmission networks
- RTCs characteristics renders possible to assess potential shifts among HIV transmission routes and populations
- This could lead, in some cases, to adapt prevention measures or to specifically target some population
- In this work, we describe the evolution of RTCs over the last decade observed through a specialized laboratory serving centers from the entire French territories

METHODS

- We extracted all the HIV reverse transcriptase sequences available from January 2013 to August 2022
- We studied the characteristics of the overall dataset and separated into three equal time periods: 2013-15, 2016-18, 2019-2021
- The first sequences available for each patient were aligned and phylogenetic trees were reconstructed by maximum likelihood using IQtree with the GTR-G nucleotide substitution model and using the ultrafastbootstrap with 1000 iteration for branch support assessment
- Clusters, defined by a maximum genetic distance < 4.5% and a branch support >90%, were extracted using ClusterPicker

Time periods	2013-15	2016-18	2019-21	*Total*
Number of identified clusters :				
≥2 séquences	298	249	226	***773***
≥3 séquences	74	67	64	***205***
≥4 séquences	21	18	33	***72***
≥5 séquences	8	4	17	***29***
≥6 séquences	4	1	8	***13***
Number of sequences included among clusters:				
Clusters ≥2	711 (19.5%)	590 (20.4%)	594 (27.5%)	***1895 (21.8%)***
Clusters ≥3	263 (7.2%)	226 (7.8%)	270 (12.5%)	***759 (8.7%)***
Clusters ≥4	104 (2.9%)	79 (2.7%)	177 (8.2%)	***360 (4.1%)***
Clusters ≥5	52 (1.4%)	23 (0.8%)	113 (5.2%)	***188 (2.2%)***
Clusters ≥6	32 (0.9%)	8 (0.3%)	68 (3.2%)	***108 (1.2%)***

Table 1. Numbers of recent transmission clusters identified among each time period.

	Sex			Mean age (years)
	Male	Female	NA	
Hors clusters :	680 (57.9%)	494 (42.1%)	389	44.4
Dans des clusters :				
Total	308 (67.7%)	147 (32.3%)	125	38.7
2 sequences	167 (67.3%)	81 (32.7%)	74	40.9
3 sequences	48 (69.6%)	21 (30.4%)	24	39.4
4 sequences	31 (62%)	19 (38%)	6	36.9
5 sequences	19 (63.3%)	11 (36.7%)	11	34.6
6 sequences	18 (94.7%)	1 (5.3%)	5	33.1
9 sequences	14 (100%)	0 (0%)	4	29.8
12 sequences	8 (72.7%)	3 (27.3%)	1	35.3
14 sequences	3 (21.4%)	11 (78.6%)	0	29.2

Table 2. Sex and age of patients included into clusters during the 2019-21 period according to the cluster size.

- Overall number of phylogenetic recent transmission clusters (RTCs) is decreasing overtime
- **But large RTCs (>4 patients) numbers are increasing**
- Large RTCs patients are younger and more frequently MSM, but largest RTC included almost exclusively young women in overseas territories
- Specific prevention efforts could be settled based on such phylogenetic analysis

RESULTS

Whole study period analysis

- Over the whole study period, 8694 sequences were included
- 950 RTCs including 2492 (29%) sequences were identified in the phylogenetic tree
  - Among them, 68 large RTCs (>4 sequences) including 475 (5.6%) sequences
  - The mean duration of large RTCs (from the first to the last sequences) was 5.1 years [IQR: 4.1-7.1]
  - 34 were still active (including at least one sequence during the last year of the study period)

Evolution of RTCs characteristics across the study period

- 3640, 2897 and 2157 sequences were belonging to the 2013-15, 2016-18 and 2019-2021 periods, respectively
- 298 RTCs (19.5% of sequences), 249 (20.4%) and 226 (27.5%) were identified for each time period, respectively
- While the number of sequence pairs decreased from 2013-15 to 2019-21, the number of large RTCs increased steadily (see Table 1)
- During the period 2019-21, including the largest clusters, patients belonging to a RTC were more often male (68 vs 58%, p< 0.001) and younger (average age: 39 vs 44 years, p< 0.001) than non-RTC patients. This observation was even more marked for very large RTCs (see Table 2)
- In the other hand, the largest cluster (14 patients) was almost exclusively composed of women and located in French overseas territories

CONCLUSIONS

- This study shows an evolution of the structure of HIV sequence clusters over the last decade in France
- We observed a decreasing number of small RTCs that can be explained by a better global control of transmission, due in part to testing measures along with prevention measures such as TasP and PreP
- Inversely, the increasing number of large RTCs (including >4 sequences) suggest that those measures are not preventing some super-transmitters networks
- The COVID period does not seem to have strongly limited such large transmission networks
- The phylogenetic measures could be of interest to detect and follow those networks as some could beneficiate of specific inquiries and targeted prevention campaigns
- This is illustrated by the largest transmission network including mainly women and observed in French overseas territories. Specific prevention campaigns better suited for those transmission networks should be developed

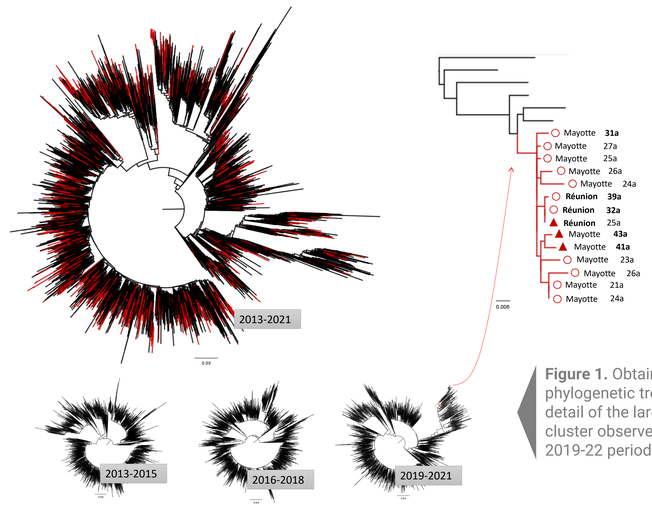

Figure 1. Obtained phylogenetic trees and detail of the largest cluster observed in the 2019-22 period.

ADDITIONAL KEY INFORMATION

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Acknowledgements

We wish to specifically thanks the teams of the University Hospital of La Réunion and Mayotte for their help and the ongoing work on the large overseas territories' networks.