Mpox Virus Sequences Diversity in Paris Area During the 2022 Outbreak

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BACKGROUND

Since May-2022, non-endemic countries reported mpox cases with no epidemiological link to Africa, mostly affecting men-who-have-sex-with-men (MSM).

We deciphered genetic variability of epidemic mpox from French infected patients and compared sequences with pre-epidemic Western-African sequences.

METHODS

Sequencing was performed on S5 Ion Torrent (ThermoFisher) device after generation of 12 amplicons (~30,000nt-outside terminal repeats; **Figure 1**).Sequences included 28/35 mutation sites previously reported in epidemic isolates compared to reference clade-3 MT903344_2018_UK_P2 pre-epidemic strain.

All 7 unexplored mutations were synonymous or non coding.

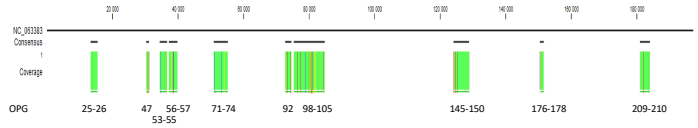


Figure 1: Distribution of amplified fragments on the genome

CONCLUSION

This rapid parsimonious mpox sequencing strategy in 148 mpox-infected patients provided a unique insight into the genomic variability of an epidemic DNA virus, confirmed the existence of epidemic strain-specific mutational patterns and quantified the overall genomic variability of circulating strains.

It highlights, although rare, the non-epidemic circulation of mpox and the need to more frequently consider mpox diagnosis.

The transition events (G to A and C to T) could suggest a role of the human APOBEC enzyme, commonly involved in other viral genome editing.

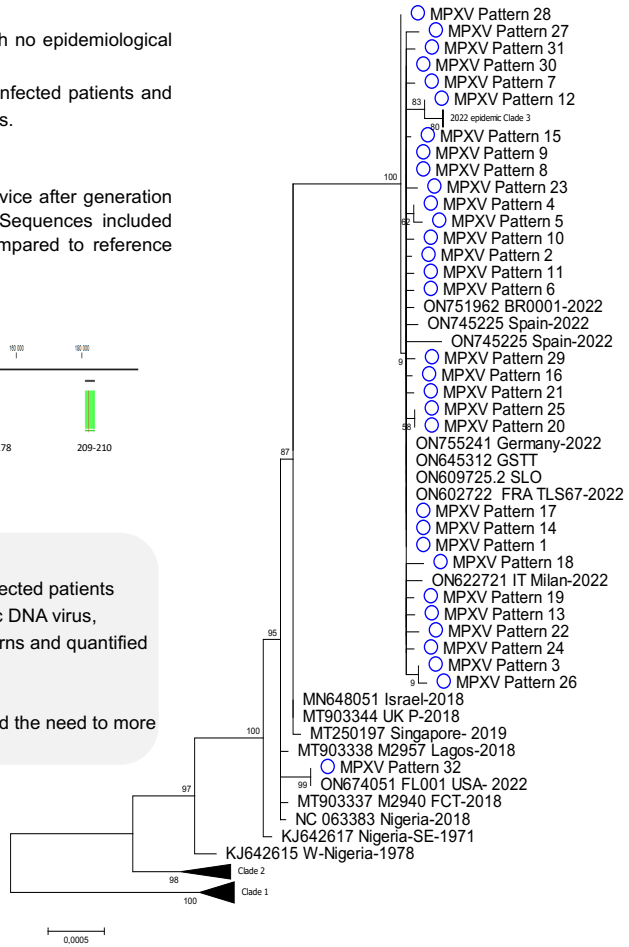


Figure 2: Phylogeny of MPXV based on the analysis of selected 30,000 nucleotides. Maximum likelihood tree using the TN93 + G model of evolution, and bootstrap analysis using 1000 pseudoreplicates. The blue circle in front of the name indicates the sequences resulting of this study.

RESULTS

We studied 148 mpox-infected patients attending Bichat University-Hospital, Paris, France:

- 128 sampled during the early 2022 outbreak period (24/05-04/07, essentially skin, buccal and anal)
- 20 later on (16/08-10/09), from which we produced 162 sequences.

Available medical records showed that 95.0% were men, 5% transgenders (M to F), and 90% MSM of whom 50% on HIV pre-exposure prophylaxis.

Among these 25% lived with HIV and 25% had travelled within 3 weeks prior to mpox diagnosis (>85% to Europe, none to Africa); 5% were hospitalized, mostly for severe pharyngeal/tonsils.

We observed 32 different mutational patterns (pattern#1 in 120 sequences; #9 in 10; and #13, #2 in 2; others in 1). All included a 17nt-deletion (pos. 150,621, intergenic) previously observed in a French sequence (ON602722) but present in only 37% of epidemic strains. Pattern#8 included a previously unreported 4nt-deletion (pos. 14,509, ORF OPG25) (**Figure 2**).

Overall, 51% of single-nucleotide mutations were non-synonymous, 37% synonymous, 12% non-coding. There was a majority of transitions (17 G to A; 17 C to T), confirming a highly specific mutational typology.

In a patient returning from Asia, we identified a profile (pattern# 32), closely related to clade-3 pre-epidemic and N674051_2022_USA. This suggests a baseline circulation of non-epidemic mpox in Western countries, probably underdiagnosed and detected here due to attention generated by the outbreak.

Mpox epidemic strain specific mutational pattern
Non epidemic circulation of mpox virus
Need to consider more frequently mpox diagnosis

ADDITIONAL KEY INFORMATION
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