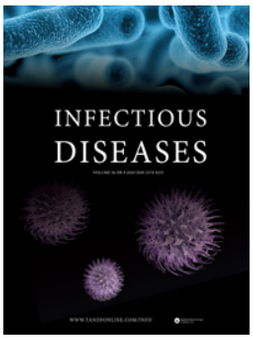

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First cases of mpox Clade I outside of Africa: genetic insights on its evolution

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COMMENT

First cases of mpox Clade I outside of Africa: genetic insights on its evolution

The recent WHO declaration reclassifying mpox (formerly known as monkeypox) [1] as a Public Health Emergency of International Significance on August 14, 2024 underscores the urgency of addressing global inequalities in access to health resources and the need for a coordinated response. This crisis is part of a broader context of global health challenges, including the Ebola outbreaks, the COVID-19 pandemic, and the 2022 mpox epidemic, which have highlighted the deep disparities in global health systems and the critical importance of community-led responses [2]. The outbreak of mpox affecting several regions of Africa in the recent period has once again highlighted the crucial importance of timely collection and sharing of epidemiological data. On August 15, 2024, the Swedish Public Health Agency reported the first case of mpox Clade I variant outside of Africa (https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/communicable-disease-control/disease-information-about-mpox/one-case-of-mpox-Clade-i-reported-in-sweden/), and less than a week later, health authorities in Thailand confirmed Asia's first case of new mpox virus strain linked to travel to Africa (https://www.cdc.gov/media/releases/2024/s0822-mpox-outbreak.html#:~:text=In%20addition%2C%20clade%20I%20mpox,with%20known%20clade%20I%20cases).

In this context, this study aims to analyse the genetic make-up of the new emerged mpox lineage, the Clade Ib. The genetic analyses have been performed by using all of the complete genomes belonging to the Clade I available in GISAID (https://www.epicov.org/epi3/frontend#d4f74) as of August 24, 2024 (see Figure S1 in Supplementary Material for details on the analysed genomes). Database was build excluding genomes with low coverage ($n = 179$). Alignment was performed by means of the L-INS-I algorithm implemented in MAFFT 7.471 [3], then manually reviewed and refined using Unipro UGENE v.35 [4] and sequences that did not provide a genomic coverage in length of at least 75% of the reference sequence were removed. The definitive dataset of 130 genomes was analysed using the Bayesian Inference by means of the software Beast 1.10.4 [5], running simulations of 200 million generations with the Coalescent Bayesian Skyline Model under a log-normal uncorrelated relaxed clock model, following the methods described by Scarpa et al. [6].

The phylogenomic reconstruction (Figure 1) indicates that all genomes belonging to Clade Ib cluster together, forming a monophyletic clade that is not evolutionarily close to other members of the clade. Its closest relative in the tree is a genome isolated in 2006 from the Democratic Republic of Congo (DRC), while other more recent genomes are widely spread across the tree. This genetic pattern is not surprising from an evolutionary standpoint, considering that the newly labelled Clade Ib is currently associated with a lower mortality rate compared to the original Clade I lineage, Clade Ia. Although there may be the absence of several unsampled genomes, Clade Ib appears to be evolving more rapidly, showing a divergence rate at the branch carrying all genomes of about 10^{-3}, compared to approximately 10^{-7} in the whole Clade I. These enhanced features give Clade Ib increased fitness, enabling the unprecedented spread of a Clade I lineage outside of African countries. Indeed, both Clade Ia and Clade Ib are present in the DRC and have been identified in neighbouring countries, as well as in Sweden and Thailand. The two extra-African cases, labelled in red on the tree, fit perfectly within the Clade Ib, which consists entirely of recent lineages from 2024 and 2023. Notably, these cases form a distinct monophyletic group within the clade, along with other genomes isolated outside DRC, specifically in Kenya and Uganda. This situation further suggests that even on a micro-geographical scale, a shift in evolutionary dynamics is necessary for successful dispersion, something that has proven to be very challenging for the older Clade Ia. However, it is interesting to note that in African countries, the new lineage has not supplanted the old one. As seen in the tree, not all genomes from 2023 and 2024 belong to Clade Ib; some still belong to Clade Ia (see Table S1 in Supplementary Material for details on the included

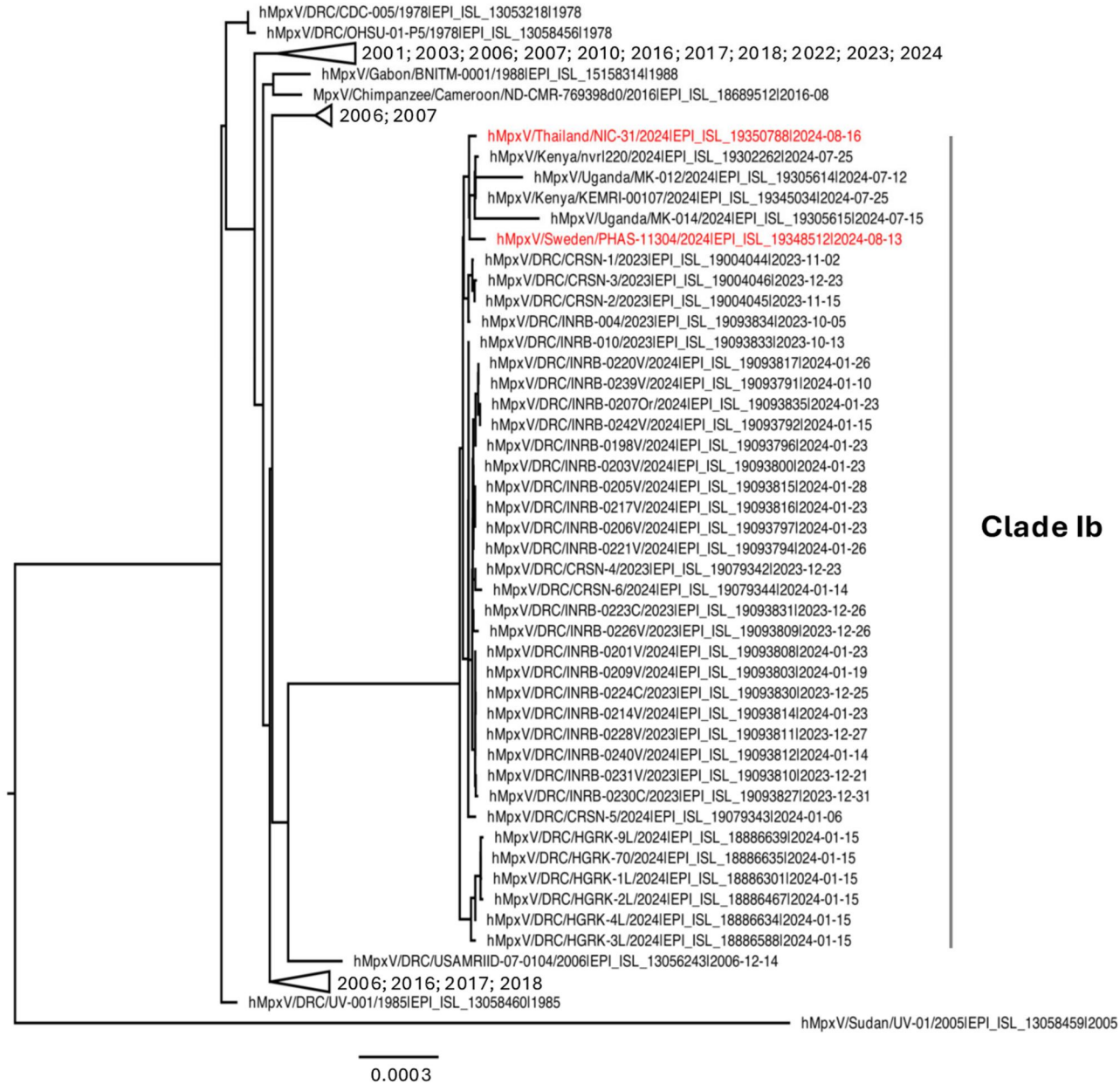

Figure 1. Bayesian phylogenomic reconstruction of the mpox Clade I virus. The branch length scale represents the number of substitutions per site. All nodes are highly supported for posterior probabilities. For details on genomes included in the collapsed clades see Table S1 in Supplementary Material.

genomes belonging to the Clade Ia). From an evolutionary standpoint, this is positive, as it suggests that, although the fitness of the new lineage has improved, it has not yet been strong enough to completely replace the ancestral lineage, which remains more stable and conserved in the area. This scenario is further supported by the lack of evidence that this variant transmits better or causes a more severe disease than Clade 1a (https://www.sciencemediacentre.org/expert-reaction-to-who-declaring-mpox-a-public-health-emergency-of-international-concern-pheic/). In fact, controlling the new lineage through enhanced prevention and information, given its modes of transmission, it might be possible to limit its evolutionary progress, effectively 'clipping its wings' in terms of spread, and causing it to become an evolutionary dead end without further descendants. Conversely, if its expansion continues unchecked, it could pose a serious problem, potentially reaching a threshold where containment and management may become very difficult.

It is crucial to continue genome-based monitoring to assess the composition and genetic variability of new cases, in order to contextualise and track their evolution in real time. This will help ensure preparedness for containment and management of the issue, and a more complete understanding will facilitate the development of predictive models.

Authors' contributions

Francesco Branda: conceptualisation, formal analysis, investigation, writing – original draft, writing – review & editing. Giancarlo Ceccarelli: investigation, writing – review & editing. Massimo Ciccozzi: validation, supervision, writing – original draft, writing – review & editing. Fabio Scarpa: conceptualisation, formal analysis, investigation, writing – original draft, writing – review & editing

Disclosure statement

The author declares that he has no competing financial interests or personal relationships that could influence the work reported in this article.

References

[1] Branda F, Romano C, Ciccozzi M, et al. Mpox: an overview of pathogenesis, diagnosis, and public health implications. J Clin Med. 2024;13(8):2234. doi: 10.3390/jcm13082234.

[2] Branda F, Ceccarelli G, Ciccozzi M, et al. Strengthening community resilience: lessons from COVID-19 for mpox prevention. Lancet (London, England). 2024. doi: 10.1016/S0140-6736(24)01752-5.

[3] Katoh K, Standley DM. MAFFT multiple sequence alignment software version 7: improvements in performance and usability. Mol Biol Evol. 2013;30(4):772–780. doi: 10.1093/molbev/mst010.

[4] Okonechnikov K, Golosova O, Fursov M, UGENE Team. Unipro UGENE: a unified bioinformatics toolkit. Bioinformatics. 2012;28(8):1166–1167. doi: 10.1093/bioinformatics/bts091.

[5] Drummond AJ, Rambaut A. BEAST: Bayesian evolutionary analysis by sampling trees. BMC Evol Biol. 2007;7(1):e214. doi: 10.1186/1471-2148-7-214.

[6] Scarpa F, Sanna D, Azzena I, et al. Genetic variability of the monkeypox virus Clade IIb B.1. J Clin Med. 2022;11(21):6388. doi: 10.3390/jcm11216388.

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