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Genetic diversity and population structure of Mpox virus in Africa: Identifying key targets for vaccine development

Abubakar Ojone Woziri[1,2,&], Ezra Ayuba[1], Asara Mohammed Abdullahi[3], Faridah Ibrahim Nasir[4], Ashafa Mustapha Aliyu[5], Maryam Aminu[5], Anyebe Bernard Onoja[6], Fatima Jumai Giwa[7], Clement Adebajo Meseko[8], Paul Habila Mamman[1], Beckie Tagbo[9,10]

[1]Department of Veterinary Microbiology, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria, Nigeria, [2]Africa Centre of Excellence for Neglected Tropical Diseases and Forensic Biotechnology (ACENTDFB), Ahmadu Bello University, Zaria, Nigeria, [3]Department of Infectious Diseases, Ahmadu Bello University Teaching Hospital, Shika, Nigeria, [4]Department of Veterinary Public Health and Preventive Medicine, Ahmadu Bello University, Zaria, Nigeria, [5]Department of Microbiology, Faculty of Life Sciences, Ahmadu Bello University, Zaria, Nigeria, [6]Department of Virology, College of Medicine, University of Ibadan, Oyo state, Nigeria, [7]Department of Medical Microbiology, College of Medicine, Ahmadu Bello University, Zaria, Nigeria, [8]Animal Influenza Division, Infectious and Transboundary Animal Diseases, National Veterinary Research Institute, Vom, Nigeria, [9]Department of Paediatrics, College of Medicine, University of Nigeria Teaching Hospital, Enugu state, Nigeria, [10]Institute of Molecular Medicine and Infectious Diseases, University of Nigeria Teaching Hospital, Enugu state, Nigeria

[&]Corresponding author: Abubakar Ojone Woziri,Department of Veterinary Microbiology, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria, Nigeria **Email:** woziriabubakar@gmail.com

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Introduction

Mpox (formerly Monkeypox) is fatal disease that is endemic in Africa, with pandemic potential. However, the genetic diversity/evolutionary patterns of Mpox virus remain underexplored. This study aimed to decipher the population genetic structure of Mpox virus and identify key virulence markers with potential as vaccine targets in Africa.

Methods

High-quality, near-full-length Mpox genome sequences of African origin (1970 – 2024; *N = 251*) were retrieved from Nextstrain and NCBI Virus databases between December, 2024 and February, 2025 (Cameroon, *n = 11*; Central African Republic, *n = 45*; Côte d'Ivoire, *n = 1*; Democratic Republic of Congo, *n = 54*; Egypt, *n = 1*; Gabon, *n = 2*; Kenya, *n = 1*; Liberia, *n = 2*; Nigeria, *n = 122*, Sierra Leone, *n = 1*; South Africa, *n = 9*; and Sudan, *n = 2*), and analyzed using high-throughput bioinformatics pipelines to determine nucleotide diversity, reassortments, phylodynamics, and conservation of key vaccine targets.

Results

Among the 944 identified mutations, 935 were polymorphic sites (singleton sites: *n = 477*; parsimony-informative sites: *n = 458*), forming 179 haplotypes with a haplotype diversity (Hd) of 0.9954 and nucleotide diversity (Pi) of 0.00232. Additionally, 55 (12.9%) indel haplotypes were identified (indel diversity = 0.775; $p < 0.001$). The genomes belonged to clades Ia (37.8%), Ib (4.8%),

IIa (1.6%), and IIb (55.8%), exhibiting significant intra-clade nucleotide variation and high inter-clade diversity. Furthermore, 34 recombination events were identified across the 251 sequences. Notably, the conservation rates of virulent genes encoding membrane (E8L, H3L, M1R) and envelope (B6R, A35R) proteins were 0% for E8L, H3L, and B6R, and 32.3% and 97.6% for A35R and M1R, respectively.

Conclusion

This study provides the first population genetic analysis of Mpox virus and highlights the M1R protein as a putative target for a potential cross-protective vaccine candidate against Mpox in Africa.