

Molecular epidemiology of recurrent zoonotic transmission of mpox virus in West Africa

Delia Doreen Djuicy*¹, Ifeanyi F. Omah*^{2,3}, Edyth Parker*^{4,5}, Christopher H Tomkins-Tinch⁶, James Richard Otieno⁷, Moïse Henri Moubeket Yifomnjou¹, Loique Landry Messanga Essengue¹, Akeemat Opeyemi Ayinla⁴, Ayotunde E. Sijuwola⁴, Muhammad I. Ahmed⁴, Oludayo O. Ope-ewe⁴, Olusola Akinola Ogunsanya⁴, Alhaji Olon⁴, Philomena Eromon⁴, Martial Gides Wansi Yonga¹, Gael Dieudonné Essima¹, Ibrahim Pascal Touoyem¹, Landry Jules Mouliem Mouchili¹, Sara Irene Eyangoh¹, Linda Ezzo⁸, Inès Mandah Emah Nguidjol⁸, Steve Franck Metomb⁸, Cornelius Chebo⁸, Samuel Mbah Agwe⁸, Hans Makembe Mossi⁸, Chanceline Ndongo Bilounga⁸, Alain Georges Mballa Etoundi¹, Olusola Akanbi⁹, Abiodun Egwuenu⁹, Odianosen Ehiakhamen⁹, Chimaobi Chukwu⁹, Kabiru Suleiman⁹, Afolabi Akinpelu⁹, Adama Ahmad⁹, Khadijah Isa Imam⁹, Richard Ojedele⁹, Victor Oripenaye⁹, Kenneth Ikeata⁹, Sophiyah Adelakun⁹, Babatunde Olajumoke⁹, Áine O'Toole², Andrew Magee¹⁰, Mark Zeller⁵, Karthik Gangavarapu⁵, Patrick Varilly⁶, Daniel J Park⁶, Gerald Mboowa¹¹, Sofonias Kifle Tessema¹¹, Yenew Kebede Tebeje¹¹, Onikepe Folarin^{4,12}, Anise Happi⁴, Philippe Lemey¹³, Marc A Suchard^{10,14,15}, Kristian G. Andersen^{5,16}, Pardis Sabeti^{6,17}, Andrew Rambaut², Chikwe Ihekweazu⁹, Idriss Jide⁹, Ifedayo Adetifa⁹, Richard Njoum¹, Christian T Happi^{4,12,17+}

*These authors contributed equally to this work

+ Correspondences: Christian T Happi (happic@run.edu.ng)

1. Virology Service, Centre Pasteur du Cameroun, 451 Rue 2005, Yaounde 2, P.O. Box 1274
2. Institute of Ecology and Evolution, University of Edinburgh, The King's Buildings, Edinburgh EH9 3FL, UK.
3. Department of Parasitology and Entomology, Nnamdi Azikiwe University, Awka, Nigeria.
4. African Center of Excellence for Genomics of Infectious Diseases, Redeemer's University, Ede, Osun State, Nigeria
5. Department of Immunology and Microbiology, The Scripps Research Institute, La Jolla, CA, USA
6. The Broad Institute of MIT and Harvard, Cambridge, MA 02142, USA
7. Theiagen Genomics, Highlands Ranch, CO, USA
8. Department for the Control of Disease, Epidemics and Pandemics, Ministry of Public Health, Yaounde, Cameroon
9. Nigeria Centre for Disease Control and Prevention., Abuja, Nigeria
10. Department of Human Genetics, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA 90095, USA
11. Africa Centres for Disease Control and Prevention (Africa CDC), Addis Ababa, Ethiopia
12. Department of Biological Sciences, Redeemer's University, Ede, Osun State, Nigeria.
13. Department of Microbiology, Immunology and Transplantation, Rega Institute, KU Leuven, Leuven, Belgium
14. Department of Biomathematics, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA 90095, USA.
15. Department of Biostatistics, Fielding School of Public Health, University of California, Los Angeles, Los Angeles, CA 90095, USA
16. Scripps Research Translational Institute, La Jolla, CA 92037, USA.
17. Department of Immunology and Infectious Diseases, Harvard T H Chan School of Public Health, Boston, MA 02115, USA

1 **Nigeria and Cameroon reported their first mpox cases in over three decades in 2017**
2 **and 2018 respectively. The outbreak in Nigeria is recognised as an ongoing human**
3 **epidemic. However, owing to sparse surveillance and genomic data, it is not known**
4 **whether the increase in cases in Cameroon is driven by zoonotic or sustained**
5 **human transmission. Notably, the frequency of zoonotic transmission remains**
6 **unknown in both Cameroon and Nigeria. To address these uncertainties, we**
7 **investigated the zoonotic transmission dynamics of the mpox virus (MPXV) in**
8 **Cameroon and Nigeria, with a particular focus on the border regions. We show that**
9 **in these regions mpox cases are still driven by zoonotic transmission of a newly**
10 **identified Clade IIb.1. We identify two distinct zoonotic lineages that circulate**
11 **across the Nigeria-Cameroon border, with evidence of recent and historic cross**
12 **border dissemination. Our findings support that the complex cross-border forest**
13 **ecosystems likely hosts shared animal populations that drive cross-border viral**
14 **spread, which is likely where extant Clade IIb originated. We identify that the**
15 **closest zoonotic outgroup to the human epidemic circulated in southern Nigeria in**
16 **October 2013. We also show that the zoonotic precursor lineage circulated in an**
17 **animal population in southern Nigeria for more than 45 years. This supports**
18 **findings that southern Nigeria was the origin of the human epidemic. Our study**
19 **highlights the ongoing MPXV zoonotic transmission in Cameroon and Nigeria,**
20 **underscoring the continuous risk of MPXV (re)emergence.**
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22 Mpox is a viral zoonosis resulting from infection with the *Orthopoxvirus* mpox virus
23 (MPXV) that is endemic in as-yet-unknown animal reservoirs in West and Central
24 Africa.^{1,2} Since MPXV was first characterized in humans in the Democratic Republic of
25 the Congo (DRC) in 1970, there have been limited outbreaks and sporadic cases in rural
26 regions of endemic countries.^{3–5} However, since 2016, there have been a marked
27 increase in mpox cases in endemic as well as non-endemic countries in Africa.² It is
28 unclear whether the increase in cases across the region is driven by increased zoonotic
29 infections, or whether MPXV may have cryptically emerged to sustained transmission in
30 the human population.^{6,7} Notably, Nigeria and Cameroon reported their first mpox cases
31 in over three decades in September 2017 and May 2018 respectively.^{5,7–9} The Nigerian
32 outbreak has now been recognised as an ongoing human epidemic, driven by sustained
33 transmission after emergence in the human population around 2014.^{10–12} MPXV has two
34 major clades: Clade 1, which is endemic to non-human animals in Central Africa, and