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Genomic characterisation of human monkeypox virus in Nigeria

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See Online for appendix

Monkeypox virus (MPXV) is a large, double-stranded DNA virus belonging to the Orthopox genus in the family Poxviridae. First identified in 1958, MPXV has caused sporadic human outbreaks in central and west Africa, with a mortality rate between 1% and 10%.¹ Viral genomes from west Africa and the Congo Basin separate into two clades, the latter being more virulent.² Recently, MPXV outbreaks have occurred in Sudan (2005), the Republic of the Congo and Democratic Republic of the Congo (2009), and the Central African Republic (2016).³

A suspected outbreak of human MPXV was reported to WHO on Sept 26, 2017, by the Nigeria Centre for Disease Control (NCDC) after a cluster of suspected cases had occurred in Yenagoa Local Government Area, Bayelsa State, Nigeria.⁴ Since the onset of the outbreak, 155 cases have been reported by the NCDC, of which 56 were confirmed.⁴ A subset of these samples was sent to the WHO Collaborating Center at the Institut Pasteur de Dakar (IPD) in Senegal for confirmation by PCR.

This was not the first report of MPXV cases in Nigeria. Between 1971 and 1978, ten human cases were reported, with three confirmed and two sequenced. Since then, no other cases have been reported in the area. Because of the lapse in MPXV cases in the region and recent cases in the Congo Basin, the origin of the Nigerian outbreak needed to be identified, as did whether the outbreak was a result of a local zoonotic spillover event or importation from another endemic country.

To help support advanced characterisation of pathogens in the region, 29 samples positive according to PCR were prepared for sequencing at IPD and enriched

using a pan-viral probe set designed by Illumina (San Diego, CA, USA) and the US Army Medical Research Institute of Infectious Diseases Center for Genomic Sciences (Frederick, MD, USA), and synthesised by Twist Bioscience (San Francisco, CA, USA). Analysis of the sequencing data found reads aligning to MPXV in 22 of the 29 samples. Three of the samples (297 957, 298 464, and 298 481) were determined to have reads covering 99.8%, 94.2%, and 95.0% of the closest related MPXV genome sequence on GenBank (a Nigeria strain, KJ642617) with average depths of 512, 56, and 25×, respectively. Reads aligned to the repetitive terminal ends but could not be used to definitely resolve the termini using the short Illumina reads.

Phylogenetic analysis (appendix) indicates that the closest relative of the three outbreak isolates were the two Nigerian strains available on GenBank (KJ642615 and KJ642617), within the west African clade. The isolates grouped most closely to KJ642617, a genome isolated from a human MPXV case in Ihie, Abia State, Nigeria, in 1971, which is relatively close to the epicentre of the current outbreak.

These findings support the hypothesis that the index case of the current outbreak in Nigeria was not imported, but probably originated from a spillover event or events involving reservoir hosts. These results emphasise the value of local surveillance for the early detection of viral spillovers and the need for advanced characterisation to help determine the origins of outbreaks.

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