PRESS RELEASE

Predominance of zoonotic transmission of the mpox virus in the Democratic Republic of the Congo

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Central Africa, especially the Democratic Republic of the Congo (DRC), is highly affected by successive mpox outbreaks. Until now, the extent of genetic diversity of the virus had not been well characterised in this region of the world. For the first time, as part of the AFROSCREEN project[1] and the PANAFPOX project[2], teams from the *Institut National de Recherche Biomédicale* (INRB) in DRC, IRD and Inserm have provided important new information on the genetic diversity of mpox virus circulating in DRC and on the predominant route of transmission. Results of this work have just been published on the Cell website on 24 October 2024.

Mpox is a viral zoonosis most likely transmitted from rodents to humans. The first case was reported in the Democratic Republic of the Congo (DRC) in 1970. This disease, which had been endemic mainly in rural and forested areas of West and Central Africa for several decades, spread around the world in 2022, including cases in European countries. For the first time, the disease has spread rapidly between individuals through sexual contact, a mode of transmission rarely observed before. This growing mpox outbreak has led to a declaration of a public health emergency of international concern.

The mpox virus can be divided into two major clades*. Clade I, the 'historical' strain of the virus, found in the Congo Basin and Central Africa, and clade II, present in West Africa, with clade IIb, found in Nigeria and responsible for the 2022 mpox outbreak.

[1] Project coordinated by ANRS MIE in partnership with IRD and the Institut Pasteur, and financed by the French Development Agency (AFD).
[2] Multidisciplinary project with a "One *Health*" approach, funded by ANRS MIE.

The most affected country is DRC, where the number of cases has doubled in recent years, rising from around 3,000 in 2021 to 5,600 in 2022, and from over 14,000 in 2023 to over 20,000 by 1st September 2024. This increase is accompanied by an alarming expansion of the geographical spread, first in eastern DRC but also in urban areas including the capital city Kinshasa, and in neighbouring countries (Rwanda, Burundi, Kenya and Uganda) previously unaffected by mpox. On 14 August 2024, the substantial rise in mpox cases led the World Health Organisation to declare the mpox outbreak a public health emergency of international concern for the second time. These new infections have been attributed to clade Ib, a new variant of clade I with increased numbers of APOBEC3** mutations, which indicate that the virus has adapted to human hosts.

The study, conducted in DRC between February 2018 and March 2024, aimed to investigate whether the rising numbers of mpox infections in the country were due to zoonotic spillovers or viral evolution linked to human adaptation and sustained human-to-human transmission. A total of of 337 viral genomes from 14 out of 26 provinces were successfully sequenced. All new sequences from the South Kivu province, in eastern RDC, corresponded to the recently described clade Ib. This variant is associated with sexual contact and sustained human-to-human transmission, and the limited genetic diversity is compatible with its emergence in 2023. All other genomes from other provinces (i.e. 95% of cases) belonged to clade Ia, which is characterised by high genetic diversity and a low number of APOBEC3 mutations compared with clade Ib. The study results therefore suggest a predominance of zoonotic transmission of mpox in the human population. The co-circulation of genetically diverse viral lineages in small geographical areas even suggests multiple zoonotic introductions over a short period from one or more reservoir species.

For the first time, a large number of clade I mpox sequences have been analysed. This study has provided important new information about the genetic diversity of mpox viruses circulating in DRC, and shows that there are two modes of transmission: zoonotic transmission (clade Ia), which predominates, and human-to-human transmission, which is emerging (clade Ib) in South Kivu and is spreading rapidly to other regions in DRC and neighbouring countries. The presence of several clade I variants in urban areas, particularly Kinshasa, also highlights the need to continue monitoring the evolution and diversity of the virus in DRC as well as its modes of transmission. It is also urgent to better document the animal reservoirs involved in zoonotic transmission.

** a group of organisms, including a particular organism and all of its descendants.*

*** APOBEC3 (Apolipoprotein B Editing Complex) are proteins that help protect against viral infections.*

Reference:

Clade I Monkeypox virus genomic diversity in the Democratic Republic of the Congo, 2018 - 2024: Predominance of Zoonotic Transmission.

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About :

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