Shailendra K. Saxena ORCID iD: 0000-0003-2856-4185

Shailendra K. Saxena ORCID iD: 0000-0003-2856-4185

SHORT COMMUNICATION

Re-emerging human monkeypox: a major public-health debacle

Shailendra K. Saxena[1,2,3,*], Saniya Ansari[1,2], Vimal K. Maurya[1,2], Swatantra Kumar[1,2], Amita Jain[1,4], Janusz T. Paweska[2,5], Anil K. Tripathi[1], Ahmed S. Abdel-Moneim[2,6,7]

[1]Centre for Advanced Research (CFAR), Faculty of Medicine, King George's Medical University (KGMU), Lucknow 226003, India.

[2]World Society for Virology (WSV), Al-Taif, Saudi Arabia.

[3]The Indian Virological Society (IVS), New Delhi, India.

[4]Department of Microbiology, King George's Medical University (KGMU), Lucknow 226003, India.

[5]Centre for Emerging Zoonotic and Parasitic Diseases, National Institute for Communicable Diseases of the National Health Laboratory Service, PB X4, Sandringham-Johannesburg 2131, South Africa.

[6]Department of Microbiology, College of Medicine, Taif University, Al-Taif 21944 Saudi Arabia.

[7]Department of Virology, Beni-Suef University, Beni-Suef 62511 Egypt.

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*** Correspondence:**

Prof. Shailendra K Saxena

Centre for Advanced Research (CFAR), Faculty of Medicine,

King George's Medical University (KGMU), Lucknow 226003, India.

Tel: 91 522 2257450; Fax: 91522 2257450;

E-mail: shailen@kgmcindia.edu

http://orcid.org/0000-0003-2856-4185

Abstract

A multi-country outbreak of the monkeypox virus has gained global attention. As of 25 May, 250 confirmed human monkeypox cases have been reported globally. Monkeypox is caused by the Monkeypox virus, which belongs to the *Orthopoxvirus* genus and *Poxviridae* family. Monkeypox is often a self-limiting infection, with symptoms lasting 2 to 4 weeks with the case fatality ratio around 3–6%. Monkeypox is transmitted to humans by direct contact with an infected person or animal or contact with virus-contaminated material. Human monkeypox infections may lead to various medical complications such as fever, rash, and lymphadenopathies. Pneumonitis, encephalitis, sight-threatening keratitis, and subsequent bacterial infections are all possible complications of monkeypox. An antiviral agent developed to treat smallpox has also been approved for use in the treatment of monkeypox in the USA. Vaccines used in the smallpox eradication program also provided immunity to monkeypox. Newer vaccines have been developed, one of which has been approved for monkeypox prevention. In this

article, we provide information about the recent outbreaks of human monkeypox, epidemiology, transmission pattern, possible diagnosis techniques, therapeutics, and available preventive strategies.

Keywords: Monkeypox, Human, Reemergence, Diagnosis, Treatment

1.1 Introduction

Monkeypox (MPX) is a viral zoonotic disease that mostly affects tropical rainforests in Central and West Africa, but can also be found in other parts of the world [1]. Monkeypox is caused by Monkeypox virus (MPXV), which belongs to *Orthopoxvirus (OPXV)* genus. Poxviruses are members of the *Poxviridae* family, a vast and diverse group with double-stranded DNA viruses that replicate in the cytosol of infected cells. When seen under an electron microscope, poxviruses exhibit brick-shaped or oval structures measuring 200–400 nm. The size ranges of MPXV are 200 by 250 nm [2]. The outer membrane protects membrane connections, as well as a tightly packed core containing enzymes, transcription factors, and a double-stranded DNA genome. The MPXV genome is made up of double-stranded linear DNA (≈197 kb), mainly composed of hairpin loops, some open reading frames, and tandem repeats, while the inverted terminal repeats (ITRs) are made up of tandem repeats, hairpin loops, and some open reading frames (ORF) (Figure 1). Despite the fact that MPXV is a DNA virus, it spends its complete life cycle in the cytoplasm of infected cells [3]. The MPXV is divided into two genetic clades: the central African, which is the Congo Basin clade, and the West African clade. The central African clade was assumed to be highly infectious and to have caused more

severe sickness in the past. The one nation where both viral clades have been detected, Cameroon, has been used to divide the two clades geographically [4]. The exploitation and control of host defences are one of the reasons for poxvirus's broad host range and subsequent evolution. The MPXV has been found to be contagious in a variety of animal species. Rope squirrels, Gambian pouched rats, tree squirrels, non-human primates, dormice, and other animals fall within this category [5].

Monkeypox is generally a short-term illness with symptoms lasting two to four weeks. The incubation time for monkeypox, or the time between infection and development of symptoms, is generally 6 to 13 days, but it can vary from 5 to 21 days [6]. The rash appears to be focused more on the face and extremities than the trunk. The inflammation can be divided into two distinct phases: the invasion period, which is marked by, intense headache, lymphadenopathy, fever, back pain, intense asthenia, and muscle aches, and the recovery period, which is marked by fever, lymphadenopathy, intense headache, muscle aches, back pain, and severe asthenia. The skin eruption generally starts one to three days after the fever appears. The cheeks, palms of the hands, and soles of the feet are all affected by monkeypox. Oral mucosal membrane, conjunctivae, genital organs, and even the cornea, are also impacted. Secondary infections, sepsis, bronchopneumonia, encephalitis, and inflammation of the cornea with resulting visual loss are all possible outcomes of monkeypox. Monkeypox has a case fatality rate that has traditionally fluctuated from 0% to 11% in the general population, with a greater rate among small children. Their incident mortality ratio has been approximately 3–6% in previous years [7].

Case definition of human monkeypox

According to the Centers for Disease Control and Prevention (CDC), the person under investigation (PUI) for MPX are individuals who are suspicious and have not been tested yet in the Laboratory Response Network (LRN). Possible cases of MPX can be explained as a person who meets one of the epidemiologic criteria and experiences fever or new rash and at least other signs and symptoms 21 days after the last exposure. The probable case of MPX is defined as a person who meets the criteria of possible MPX case along with new rash with or without fever. In addition, the probable case includes the presence of detectable levels of anti-orthopoxvirus IgM antibody during 4 to 56 days after the onset of rash. Whereas, the confirmed orthopoxvirus case is defined as the person who meets the possible case definition and demonstrates the PCR positive for orthopoxvirus DNA or demonstrates the presence of orthopoxvirus by immunohistochemistry or electron microscopy. The confirmed monkeypox cases are defined as the person who meets the possible case definition along with presence of monkeypox virus DNA by PCR or next-generation sequencing of clinical samples or isolation of MPXV in culture from a clinical specimen [8].

Outbreaks of monkeypox

MPXV was initially discovered in monkeys held at a research centre in Copenhagen, Denmark, in 1959 as an epidemic of a pox-like illness [9]. Human monkeypox was discovered in a 9-year-old kid in the Democratic Republic of Congo in 1970, in a location where smallpox had already been controlled in 1968. Since

then, the majority of the cases were recorded from the Congo Basin's rural, rainforest regions, mainly in the Democratic Republic of Congo, and human outbreaks were reported throughout Central and West Africa [10]. MPX has been documented in 11 African nations since 1970: Cameroon, Benin, Central African Republic, Gabon, Democratic Republic of Congo, Nigeria, Cote d'Ivoire, Liberia, Sierra Leone, Republic of Congo, and South Sudan. MPX is a worldwide public health concern since it affects not only countries in Central and West Africa, but also the entire world [11]. Over Seventy incidences of MPX were documented in the United States as a result of this epidemic. Travelers from Nigeria to Israel in September 2018, the United Kingdom in December 2019, May 2021, and May 2022, Singapore in May 2019, and the United States of America in July and November 2021 have mostly been confirmed to have monkeypox. Additional outbreaks of MPX were confirmed throughout many non-endemic countries in May 2022 [12].

Epidemiology of monkeypox

Since early May, 2022 a monkeypox outbreak has been spreading across many countries. A number of 9 incidents have been reported in the United Kingdom since the infection was first reported on May 7, 2022. According to the European Centre for Disease Prevention and Control, the UKHSA (UK Health Security Agency) reported a familial cluster of two cases of monkeypox in the United Kingdom (UK) on 14 May 2022 [13]. A record of 219 known cases has been documented from nations where the infection is not considered endemic as of May 25, 2022. Australia (2), Argentina (1 suspected case), Canada (15), the United Kingdom (71), Israel (1),

Switzerland (2), the United States (9), the United Arab Emirates (1 with a travel history to West Africa), and Morocco are among the countries reporting cases outside the EU/EEA (3 suspected cases) (Figure 2A, B) [14,15]. These recently re-emerged strains of MPXV were analyzed based on the numbers of mutations and found to be genotypically distinct from their predecessor's strains of MPXV (Figure 3) [16].

Transmission of Monkeypox virus

MPXV transfer can take place in two ways: from animals to humans or from humans to humans. Inter-human transmission has been attributed to respiratory droplets and exposure to bodily fluids, as well as infected patients' surroundings and sick person's skin sores [17]. Immediate contact with the blood, body fluids, or epidermal or mucosal lesions of infected animals can result in pandemic (animal-to-human) transmission. Many animals in Africa have been reported to have been infected with the MPXV, including rope squirrels, Gambian pouched rats, tree squirrels, dormice, and others. Monkeypox's natural reservoir has yet to be established, while rats are the most likely suspect [18]. Close contact with respiratory secretions, skin sores of an infected person, or previous objects that are contaminated can result in human-to-human transmission. Transmission via droplet respiratory particles usually requires prolonged face-to-face contact, which puts health workers, household members, and other close contacts of active cases at greater risk [19]. In addition, zoonotic transmission could occur by direct contact

with the blood, body fluids, and inoculation from mucocutaneous lesions of an infected animal. [20].

Diagnosis for monkeypox

MPXV infections have various clinical signs and symptoms that are closely related to smallpox, chickenpox, measles, bacterial skin infections, scabies, medication allergies and syphilis. Therefore, an early differential diagnosis is important to recognizing and restricting the virus spread to the community. In laboratory, MPXV can be diagnosed by using techniques like viral culture/isolation, polymerase chain reaction (PCR, real-time PCR), electron microscopy, immunohistochemistry and serological analysis for specific antibodies (IgG and IgM based) [21]. Although, serology and antigen-based methods are not recommended for diagnosis due to the cross-reactivity with other *Orthopoxviruses*. Among the diagnostic tests, PCR is the preferred laboratory test given its accuracy and sensitivity. According to the WHO, the confirmation of MPXV infection depends on the nucleic acid amplification testing (NAAT), using real-time or conventional polymerase chain reaction (PCR), for detection of distinct sequences of viral DNA. For diagnosis of MPX, PCR can be performed alone, or in combination with sequencing [22]. The primers/probes sequence for the panPox-real time PCR has been developed which are listed in Table 1 [23]. In addition, some detection assays have been developed which are specific toward MPXV Congo Basin strain and MPXV West African strains along with a generic MPXV that works on broad range [24]. Apart from this, recent studies have demonstrated that antiviral antibody and T-cell

response increases at the time of infection, indicating that development of new highly sensitive immunological approaches might enhance MPX detection during an epidemic [25]. Changes in the Monkeypox virus MPXV-BY-IMB25241 genome sampled during May 2022 have been listed in Table 2 [16].

Antivirals for monkeypox

Currently, no antiviral drug is licensed for the treatment of human monkeypox infection. Monkeypox clinical management should be properly adjusted in order to reduce symptoms, manage complications, and minimize long-term consequences. To maintain proper nutritional status, patients should be given water and food. Secondary bacterial infections should be treated according to the guidelines [26]. Recently, European Medical Association (EMA) has licensed the Tecovirimat for the treatment of monkeypox in 2022 based on findings from animal and human data indicating the drug was safe and tolerable with only minor side effects. Tecovirimat is not generally available and primarily designed for the treatment of smallpox. Cidofovir and Brincidofovir have proven activity against poxviruses in in vitro and animal studies. However, currently no evidence is available to claim the effectiveness of both the drugs for the treatment of human cases of monkeypox. Similarly, Vaccinia Immune Globulin (VIG) was also tested for the treatment of monkeypox infection. However, its effectiveness against monkeypox in human subjects is still not well established [27].

Vaccines for monkeypox

Several observational studies have shown that smallpox vaccination is nearly 85 percent effective in preventing monkeypox. As a result, earlier vaccination against smallpox may result in a milder sickness during monkeypox infection. In 2019, a novel vaccine based on a modified attenuated Vaccinia virus (Ankara strain) was authorized for monkeypox prevention. This is a two-dose vaccine that is still in short supply. Due to the cross-protection afforded by the immune response to *Orthopoxviruses*, smallpox and monkeypox vaccines are created in formulations based on the Vaccinia virus [28, 26, and 27]. In the United States, JYNNEOS™ (also known as Imvamune or Imvanex) has been approved to prevent monkeypox and smallpox. A clinical investigation on the immunogenicity of JYNNEOS™ and efficacy data from animal studies was used to determine the effectiveness of JYNNEOS™ against monkeypox. Another vaccine called ACAM2000, which includes a live Vaccinia virus, is approved for use in adults over the age of 18 who are at high risk for getting smallpox. This vaccine also provides protection against monkeypox [29, 26 and 27].

Conclusions and future perspectives

Monkeypox is a zoonosis caused by the monkeypox virus, an orthopoxvirus related to the smallpox virus. It was initially discovered in Central Africa in 1970 and has historically afflicted some of the world's poorest and most marginalized people. Fever, rash, and lymphadenopathy are all symptoms of the clinical condition. Pneumonitis, encephalitis, sight threatening keratitis, and subsequent bacterial

infections are all possible complications of monkeypox [30]. The human-to-human transmission of monkeypox is well documented, including nosocomial and household spread. There are currently no approved treatments for human monkeypox; however, in the United States, two orally bioavailable medicines, Brincidofovir and Tecovirimat, have been approved. Although vaccines are available, studies have shown that smallpox vaccination is nearly 85 percent effective in preventing monkeypox. Monkeypox control strategies should emphasize intersectoral coordination, but not necessarily under the One Health umbrella. Future research and studies should focus on integrative techniques that combine human, animal, and environmental efforts to better understand the diverse parts of this disease system and offer appropriate solutions to preserve public health.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

AUTHOR CONTRIBUTIONS

Shailendra K. Saxena conceived the idea and planned the study. Saniya Ansari, Vimal K. Maurya, Swatantra Kumar and Shailendra K. Saxena collected the data, devised the initial draft, reviewed the final draft, and contributed equally to this study as the first author. Shailendra K. Saxena, Saniya Ansari, Vimal K. Maurya, Swatantra Kumar, Amita Jain, Janusz T. Paweska, Anil K. Tripathi, and Ahmed S. Abdel-Moneim finalized the draft for submission. All authors read and approved the final version of the manuscript.

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COMPLIANCE WITH ETHICAL STANDARDS

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

ORCID

Shailendra K. Saxena http://orcid.org/0000-0003-2856-4185

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Figures

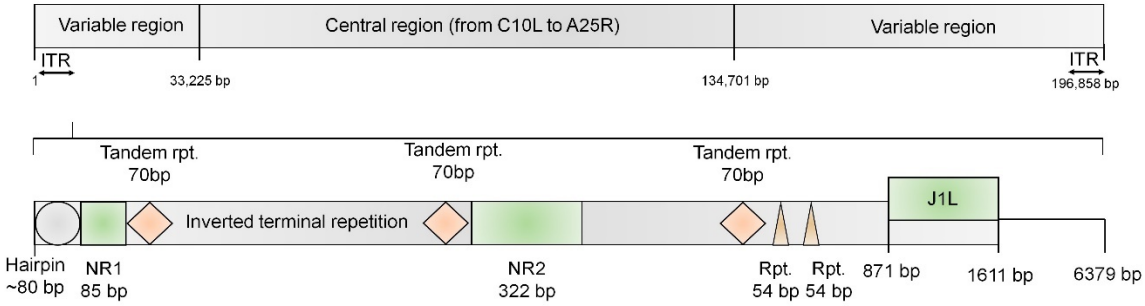

Figure 1: Genomic organization of Monkeypox virus (MPXV). MPXV genome is ~197kb in length where the central genomic region comprises of 101,476 bp. Both

the terminal ends have a 6379 bp terminal inverted repetition (ITR), a hairpin of 80bp, 54 bp short tandem repeats, NR1 and NR2 regions and the coding region.

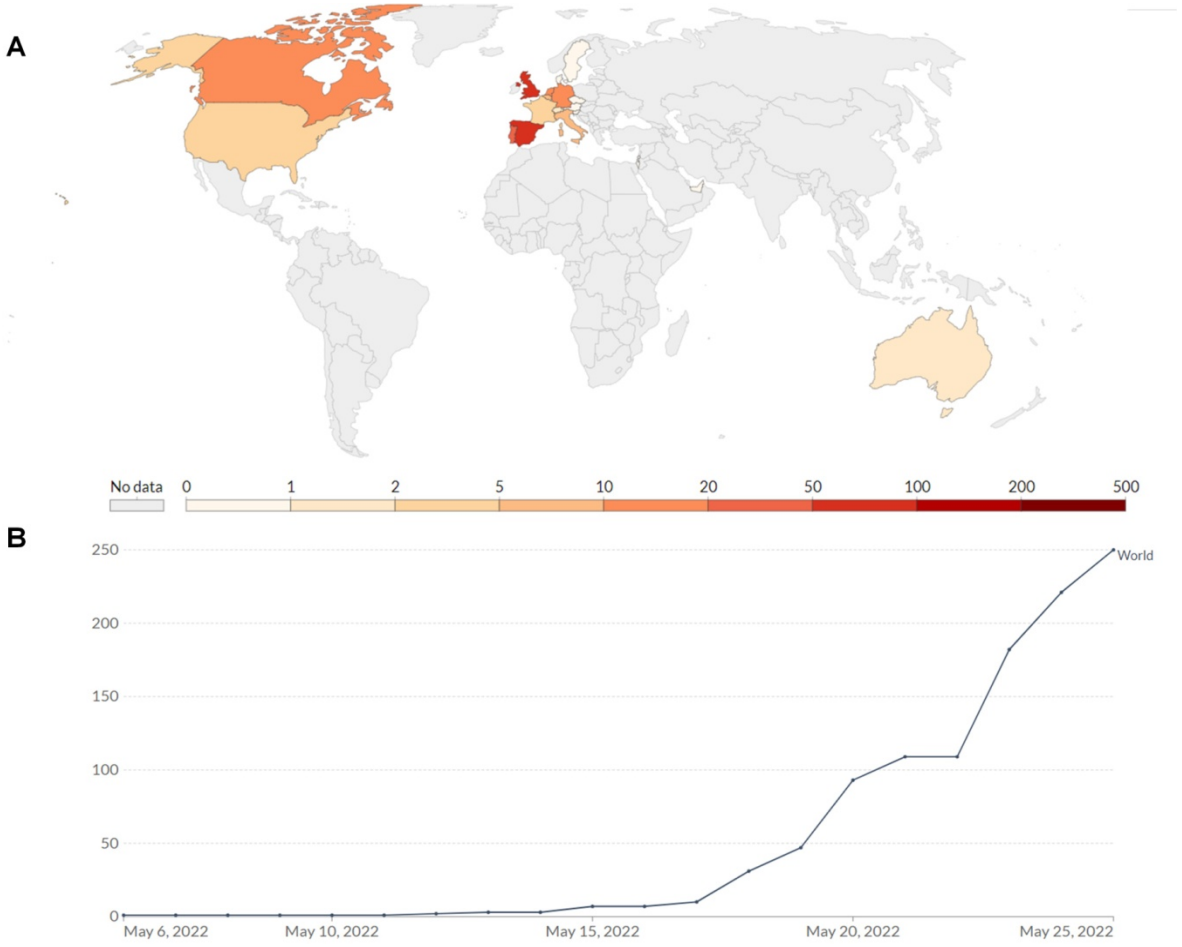

Figure 2: Recent global epidemiology of Monkeypox. A. World map is showing the recent outbreaks of Monkeypox virus (MPXV) where the cases are predominantly reported in Europe, United states and Australia. The color coding is showing the number of the conformed cases in that area. **B.** Recent global trend in the number of cumulative conformed cases of Monkeypox [15].

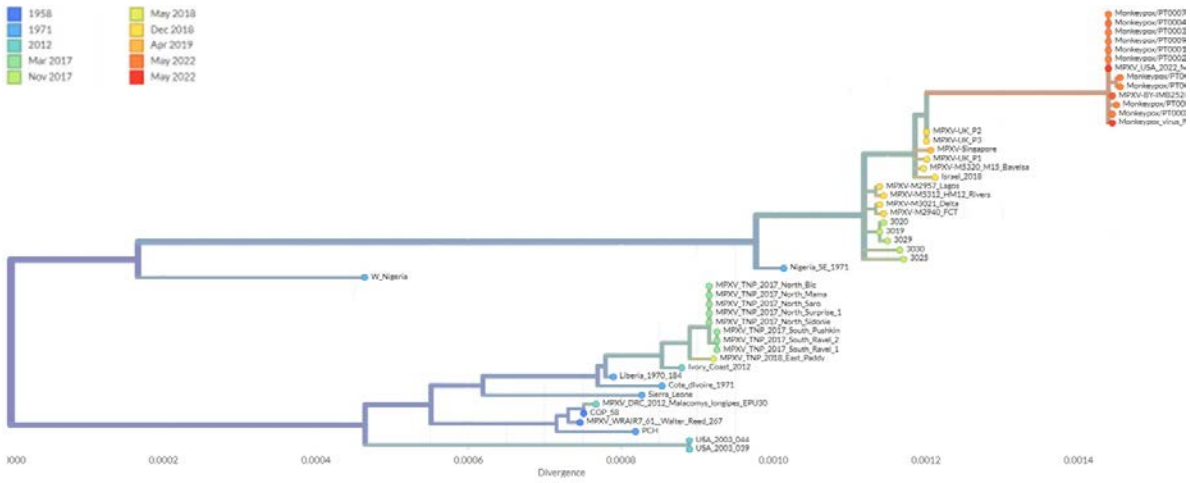

Figure 3: Phylogenetic tree showing the mutational divergence of recently re-emerged Monkeypox virus (MPXV). Sampling date wise divergence among these re-emerged MPXV was evaluated based on the number of mutations showing that the recently re-emerged MPXV strains are genotypically distinct from the predecessors' strains. Strains are denoted as specific color dots showing its year wise occurrence and the tips are labeled as the sample name on Nextstrain [16].

Table 1: Primers/probes sequences for the diagnosis of Monkeypox virus (MPXV) real-time PCR.

MPXV West African specific (G2R_WA) assay [24]	
Forward primers	5'-CACACCGTCTCTTCCACAGA-3'
Reverse primers	5'-GATACAGGTTAATTTCCACATCG-3'
Probes	5'-**FAM**-AACCCGTCGTAACCAGCAATACATTT-**BHQ1**-3'
MPXV Congo Basin specific (C3L) assay [24]	

Forward primers	5'-TGTCTACCTGGATACAGAAAGCAA-3'
Reverse primers	5'-GGCATCTCCGTTTAATACATTGAT-3'
Probes	5'-**FAM**-CCCATATATGCTAAATGTACCGGTACCGGA-**BHQ1**-3'
MPXV generic (G2R_G) assay [24]	
Forward primers	5'-GGAAAATGTAAAGACAACGAATACAG-3'
Reverse primers	5'-GCTATCACATAATCTGGAAGCGTA-3'
Probes	5'-FAM-AAGCCGTAATCTATGTTGTCTATCGTGTCC-3'-BHQ1
panPox-real time PCR primers/probes [23]	
Forward primers	F1:5'-CCDCAYCARYTVGCIACIBTIGAYT-3'
Reverse primers	R1:5'-GMDATIAYIGTYTTICCTGAICCCAT-3' R2:5'-GCCACGAATGTCTTACCACTTCCCAT-3'
Probes	A: 5'-**FAM**-WYRTGAAAYAWYADDRCDST-**MGB**-3' E: 5'-**FAM**-TYATGAAAYADYAWNRCWYT-**MGB**-3' C: 5'-**FAM**-ATRTGRAAHARYARHACRCTYYTRT-**MGB**-3' hGC: 5'-**FAM**-ATGTGRAASAGVARSAYRCT-**MGB**-3'

Table 2: Sequence changes observed (from root) in human Monkeypox virus MPXV-BY-IMB25241genome sampled during May 2022 [16].

MPXV-BY-IMB25241	
Collection date	2022-05-19
Host	Human
Outbreak Associated	Yes
Country	Germany
Region	Europe
Accession	ON568298
Sequence changes observed (from root):	
Nt	**Changes (391):** G3108T, G3120A, G3429A, G3459A, G3531A, C3827T, A4700G, -4702C, -4703T, -4704T, -4730A, -4731T, -4732G, C7780T, C8902A, G14009T, G15437A, G18321A, C19376T, G21732A, C23573T, G25670A, G30376A, G31062A, -32218G, -32219A, -32220C, C33052T, C33152T, -33202A, -33417T, C33972T, T34014C, G34304A, G34468A, C34694T, T35868C, T36741C, G37211A, G38076A, G38369A, C38671T, C39128T, C39148T, G46904A, A48147G, C48536A, G52894A, C53216A, G54126A, G54644A, A55759G, C55814T, C58476T, T58491G, G64306A, G66589A, C70407A, C72371T, C73075T, G73248A, G74214A, G77392A, C80995T, G81284A, C82382T, G82460A, C83335T, C84596T, G87239A, G87306A, G91737A, T92525C, G95043A, G99221A, G99692A, C100571T, G104994A, T105135C, C106124T, A107241G, T107375G, T107403C, G109391A, A109589G, C119305T, C121329T, G124139A, G124683A, C124746T, C124997G, G125258A, T125523G, G126264A, G128085A, C128707T, C130855T, G131557A, C132728A, -132820T, T133550C, A133693G, C133744T, C133977T, G134895A, G135717A, A136457G, G136509A, -136566T, -136569G, G136615A, C136652T, G136698A, G136881A, G137526A, G137638A, -140116A, -140117T, -140118A, -140119A, -140120C, -140121A, -140122A, -140123T, -140124T, A140783G, G141311A, C141375T, A142348G, C142461A, T146698C, C147871T, T147937A, G148135A, A148137G, G148423A, T148553C, A149889G, C150480T, A151472C, A153221C, G154416A, G155806A, T156092C, A156173C, -156425C, -156426A,

	C156437T, A156459G, G156523A, -156557A, -156558G, G156965A, C156989T, T157284G, T157291C, G157448A, C157501T, -157683A, -157684T, -157685G, -157686A, -157687T, -157688A, -157689A, -157690A, -157691A, -157692A, -157693T, -157694T, -157695T, -157696T, -157697A, -157698A, -157699G, -157700C, -157701G, -158038A, -158039T, -158040A, -158177A, C158186A, G158409A, G158414A, G158522A, G158679T, T158992C, G159426A, A159458C, T159975G, T160131C, C160163T, G160878A, C161585T, A161771G, G161810A, G162254A, G162302A, C162342T, C162839T, -163202A, -163203A, -163206A, -163207A, C163478T, C164843T, C164859T, C165315T, -166102A, -166103A, -166104T, -166105A, -166106A, -166107T, -166108T, -166109A, -166110A, -166111T, -166112A, -166113A, -166114T, -166115T, G166410T, -166666T, -166667T, T167137C, G167667T, C167869T, C168131T, C168288A, -168453T, -168454A, C168599G, G169585A, G169614A, -169820A, -169821A, -169822G, G170259A, G170273A, A170294G, G170446A, -170925G, A171079G, G171686A, -172090T, G172199A, C172535T, G172991A, G173161A, -173357A, -173358T, -173359A, -173360T, -173361A, -173362T, -173363A, -173364T, -173365A, -173366T, -173367A, -173368T, -173369A, -173370T, -173371A, -173372T, -173373A, -173374T, -173375A, -173376T, -173377A, -173378T, -173379A, -173380T, -173381A, -173382T, -173383A, -173384T, -173385A, -173386T, -173387A, -173388T, -173389A, -173390T, -173391A, -173392T, -173393A, -173394T, -173395A, -173396T, -173397A, -173398T, -173399A, -173400T, -173401A, -173402T, -173403A, -173404T, -173405G, C173528T, -173585T, -173586A, A173631G, A173728G, -173827T, G173896A, C173897T, T173969C, C174257T, -174606G, -174607A, -174608T, -174609G, -174610A, -174611A, -174612G, -174613A, -174614T, -174615G, -174616A, -174617A, A175152C, A175483G, C176247T, G177160A, G177254T, G178220A, C178362T, T178372C, G178482A, G178510A, G178627A, A178974G, A179159T, T179163G, T179438C, -180484A, -180485A, -180486A, -180487A, -180488A, -180489A, -180490T, -180491T, A181091G, -181117T, -181118A, -181119T, -181120A, -181121T, -181122T, -181123C, -181124C, -181125T, -181261A, G181365A, G181995A, G182009A, A182426C, G182458A, G182506A, T182615C, C183023T, C183534T, G183710A, C183711T, G184152A, G186593A, C187169T, C187443T, T189288C, G189433A, -

	189754T, G189826T, G190113T, A190787C, -192501T, -192502C, -192503A, -192530A, -192531A, -192532G, T192534C, G193407A, C193703T, C193775T, C193805T, C194114T, C194126A, C194634T, C195963T **Reversions to root (28):**T146873T, A146874A, T146875T, T146876T, T146877T, T146878T, A146879A, T146880T, A146881A, T146882T, T146883T, T146884T, T146885T, A146886A, T146887T, A146888A, T146889T, T146890T, T146891T, T150569T, G150571G, A150572A, T150573T, A150574A, T150575T, G150576G, A150577A, T150578T **Gaps (3 regions, 68bp):** 173285..173293 (9 bp), 173325..173356 (32 bp), 179164..179190 (27 bp)
MPXV-UK_P2-003	Changes (1):D264N
MPXV-UK_P2-012	Changes (1):A423D
MPXV-UK_P2-025	Changes (1):S36F
MPXV-UK_P2-031	Changes (1):R48C
MPXV-UK_P2-033	Changes (4):V37M, X314R, X315H, X319*
MPXV-UK_P2-034	Changes (3):X1M, X72F, X76*
MPXV-UK_P2-037	Changes (1):P78S
MPXV-UK_P2-038	Changes (1):G438R
MPXV-UK_P2-039	Changes (1):T118A
MPXV-UK_P2-040	Changes (2):E125K, A323V
MPXV-UK_P2-041	Changes (1):E353K
MPXV-UK_P2-055	Changes (2):L108F, W411L
MPXV-UK_P2-056	Changes (1):D56N
MPXV-UK_P2-058	Changes (2):V441I, F459S
MPXV-UK_P2-067	Changes (1):R620Q
MPXV-UK_P2-072	Changes (1):A178E

MPXV-UK_P2-075	Changes (1):D196N
MPXV-UK_P2-076	Changes (2):S30L, D88N
MPXV-UK_P2-077	Changes (1):M142I
MPXV-UK_P2-081	Changes (1):E162K
MPXV-UK_P2-087	Changes (1):A12T
MPXV-UK_P2-088	Changes (1):S734L
MPXV-UK_P2-092	Changes (1):H740Y
MPXV-UK_P2-101	Changes (2):R256K, S413N
MPXV-UK_P2-106	Changes (1):A29V
MPXV-UK_P2-108	Changes (2):N97H, V514I
MPXV-UK_P2-119	Changes (1):D98N
MPXV-UK_P2-122	Changes (1):A17T
MPXV-UK_P2-128	Changes (5):E62K, R243Q, T264I, P348A, E435K
MPXV-UK_P2-133	Changes (2):D100N, S307L
MPXV-UK_P2-137	Changes (7):T14M, A343T, T355I, X370I, X371I, Y408H, X510*
MPXV-UK_P2-143	Changes (5):X113N, -114N, -115N, X116Y, X146*
MPXV-UK_P2-145	Changes (2):E67K, A88V
MPXV-UK_P2-147	Changes (1):I46V
MPXV-UK_P2-151	Changes (1):D31G
MPXV-UK_P2-153	Changes (2):T145M, V167D
MPXV-UK_P2-154	Changes (1):A30T
MPXV-UK_P2-155	Changes (1):Y285C
MPXV-UK_P2-157	Changes (2):N24D, H221Y
MPXV-UK_P2-161	Changes (2):G14R, G66V

MPXV-UK_P2-162	Changes (3):I22T, A167T, E177D
MPXV-UK_P2-165	Changes (1):R506C
MPXV-UK_P2-167	Changes (4):C80F, X165Y, X166F, X169*
MPXV-UK_P2-169	Changes (2):R108I, L263F
MPXV-UK_P2-170	Changes (4):X71V, X72I, S120C, X222*
MPXV-UK_P2-171	Changes (3):X47K, X48E, X101*
MPXV-UK_P2-172	Changes (2):D71N, R133Q
MPXV-UK_P2-173	Changes (1):E230K
MPXV-UK_P2-175	Changes (2):C99Y, A156T
MPXV-UK_P2-176	Changes (2):M5I, H6Y
MPXV-UK_P2-177	Changes (2):K178N, K289E
MPXV-UK_P2-178	Changes (2):R169W, R473H
MPXV-UK_P2-179	Changes (3):P39S, V42A, V79I
MPXV-UK_P2-180	Changes (1):I53T
MPXV-UK_P2-181	Changes (1):R187G
MPXV-UK_P2-182	Changes (7):D209N, R363H, G379D, P722S, P781S, A928T, M1741I
MPXV-UK_P2-184	Changes (1):D74N
MPXV-UK_P2-185	Changes (1):R1M
MPXV-UK_P2-186	Changes (1):E121D
MPXV-UK_P2-188	Changes (1):D264N
MPXV-UK_P2-189	Changes (1):S54F
MPXV-UK_P2-190	Changes (1):S105L