

## Description of Supplementary Data

**File name: Supplementary Data 1. NovaSeq sequencing quality control values**

**File name: Supplementary Data 2. Low-complexity regions (LCRs) in the monkeypox virus (MPXV) high-quality genome (HQG) sequence 353R**

Listed are annotated positions (according to the reference MPXV-M5312\_HM12\_Rivers isolate genome sequence), sequence, and flanking regions of each area, as described previously [114](#). ID, identification; STR, short tandem repeats.

**File name: Supplementary Data 3. Short tandem repeats (STRs) in low-complexity regions (LCRs)**

Detailed information on STRs of the entire dataset used for analysis in **Figure 2**.

**File name: Supplementary Data 4. Phylogenetic analysis**

Detailed information on groups depicted in **Figure S2**. SNP, single-nucleotide polymorphism.

**File name: Supplementary Data 5. Genome sequences used in the study**

GI, genome identifier; NA, not applicable.

**File name: Supplementary Data 6. Characterization and validation of non-randomly distributed low-complexity regions (LCRs) in the monkeypox virus (MPXV) 353R genome sequence**

Detailed information on the represented materials, along with originator and epidemiological data, used for analysis in **Figure 2**. SRA, Sequence Read Archive (SRA); ID, identification; QC, quality control.

**File name: Supplementary Data 7. Single-nucleotide polymorphism (SNPs) called against the subclade IIb lineage A reference isolate MPXV-M5312\_HM12\_Rivers genome sequence for subclade IIb lineage B.1 353R and MPXV\_USA\_2022\_MA001 genome sequences.**

**File name: Supplementary Data 8. Top Early differentially expressed MPXV genes.**

Wald test performed in DESEQ analysis. *p*-values were corrected by Benjamini–Hochberg (BH) adjustment, *p*-values indicated in last column.