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RAPID REVIEW

Genomic Epidemiology and Molecular Characteristics of Bundibugyo Virus

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Key Findings

The 2026 outbreak of Bundibugyo virus (BDBV) in the Democratic Republic of the Congo (DRC) and Uganda represents a significant public health emergency with 909 suspected cases, 119 suspected fatalities, and 11 confirmed fatalities reported as of May 24, 2026.[1] This review highlights the genomic and molecular characteristics of BDBV, focusing on mutations identified in recent and past outbreaks.

- Comparative genomic analyses based on current available genomic sequences indicate that the 2026 outbreak likely originated from a novel zoonotic spillover event rather than direct continuation of the 2007 Uganda or 2012 DRC outbreaks[2].
- Based on genomic analysis, shared nonsynonymous substitutions, concentrated in antigenically exposed regions of the glycoprotein (GP) gene, were observed in the 2012 and 2026 outbreak genomes. Additional substitutions identified exclusively in the 2026 genomes occurred in GP and other genes (Table 1).
- There is currently no experimental evidence that the identified substitutions alter viral transmissibility, pathogenicity, or viral fitness.

Scope

Public Health Ontario is providing evidence-based information based on current evidence on the BDBV to understand whether any recent changes in the viral genome may alter or enhance its ability to transmit person-to-person. This report summarizes current knowledge of the genomic epidemiology and molecular characteristics of the BDBV (*Orthoebolavirus bundibugyoense*) implicated in a Bundibugyo virus disease (BVD) outbreak in the DRC and Uganda. The analysis described here includes recently sequenced BDBV virus genomes from the patient isolates released on the open-source database Pathoplexus.

Background

Orthoebolaviruses are filoviruses that cause severe hemorrhagic fever in humans and non-human primates. Four of the six *Orthoebolavirus* species can cause haemorrhagic fever in humans with high fatality rates ranging from 25-90%.[3,4] *Orthoebolaviruses* are zoonotic pathogens that are transmitted through indirect or direct contact with blood or bodily fluids. Index patients can have contact with a wide range of animal hosts such as chimpanzees, gorillas, olive baboons, and bats all of which have been implicated with prior outbreaks. Fruit bats are the suspected primary reservoir for BDBV. BVD caused by BVBD, has a fatality rate of 32% and 34% from previous outbreaks in 2007 (Uganda) and 2012 (DRC), respectively. Currently there are no vaccines or therapeutics for BDBV, but supportive care can improve case outcomes.[3-6]

On May 5, 2026, the World Health Organisation (WHO) was alerted of a high-mortality disease outbreak in the Ituri province of the DRC. On May 15, 2026, laboratory analysis confirmed cases of BDBV (*Orthoebolavirus bundibugyoense*), a species of Ebola virus.[7] On May 17, 2026, it was declared a public health emergency of international concern by the WHO.[8] As of May 24, 2026, there are 909 suspected cases with 119 suspected fatalities and 11 confirmed fatalities.[1]

Methods

We reviewed the published and preprint literature for BDBV mutations potentially associated with outbreak dynamics and viral evolution. PubMed searches were performed using combination of the following keywords: ("Bundibugyo virus" OR "Bundibugyo ebolavirus" OR " *Orthoebolavirus bundibugyoense* " OR BDBV) AND (genome OR genomic OR sequencing OR phylogenetic OR molecular OR SNP OR mutation OR substitution) OR (outbreak OR cluster OR spillover) Sequence data from the 2026 outbreak and previously reported outbreak-associated sequences (n=54) were retrieved from the SeqSet [9] and analyzed for genomic relatedness.

Results

Characteristics of Bundibugyo virus (BDBV)

BDBV is a filamentous enveloped, single-stranded, negative-sense RNA virus. It has a non-segmented genome (~19kb) that encodes seven genes[4,10-12]:

- Nucleoprotein (NP) is responsible for regulating viral gene expression, binding and protecting the viral genome, and is part of the nucleocapsid (with viral RNA) that plays a role in viral assembly during replication within a host.
- VP35 protein is essential for viral replication, transcription, and evasion of the host immune response.
- VP40 protein is another multifunctional protein with roles in budding the virus from a host cell's plasma membrane, virion assembly, and transcription.
- Glycoprotein (GP) is a critical gene in BDBV disease and encodes four proteins:
  - The entire gene encodes a glycoprotein with two subunits, GP1 and GP2. GP1 binds to the host cells and in combination with GP2, fuses with host cells to release virion content in the cell. GP is highly glycosolated which helps the virus evade the immune response.
  - Soluble secreted glycoprotein (sGP) is secreted outside host cells and is hypothesised to inhibit function and production of certain immune cells. The associated delta peptide, a cleavage product of sGP, may also contribute to pathogenesis by acting as a viroporin that disrupts host cell membranes and promotes cytotoxic and enterotoxin effects.
  - Shed glycoprotein (shed GP) is secreted from host cells in large quantities during infection. It functions as an antigen decoy or sink by absorbing specific antibodies. Shed GP is also associated with cytokine production.
  - Soluble small secreted glycoprotein (ssGP) is thought to inhibit immune response and aim immune evasion. It is present in the bloodstream of infected individuals.
- VP30 encodes a protein with critical roles in viral replication as well as the initiation and regulation of viral transcription.
- VP24 encodes a protein critical for the formation of the nucleocapsid. It is also associated with the inhibition of host interferon responses.
- L encodes a large five-unit RNA polymerase which is crucial to viral replication within host cells. It forms a replication complex with NP, VP30, and VP35.

Prior to the current BDBV outbreak in the DRC and Uganda, there were two previous outbreaks of BDBV in 2007 and 2012. The 2007 BDBV outbreak in Uganda had 131 reported cases with 42 fatalities (32%) and the 2012 BDBV outbreak was in the DRC with 38 lab confirmed cases and 13 fatalities (34%).[13]

The genomic analysis indicates the 2026 outbreak likely originated from a new zoonotic spillover, not directly from the 2007 or 2012 outbreaks.[2]

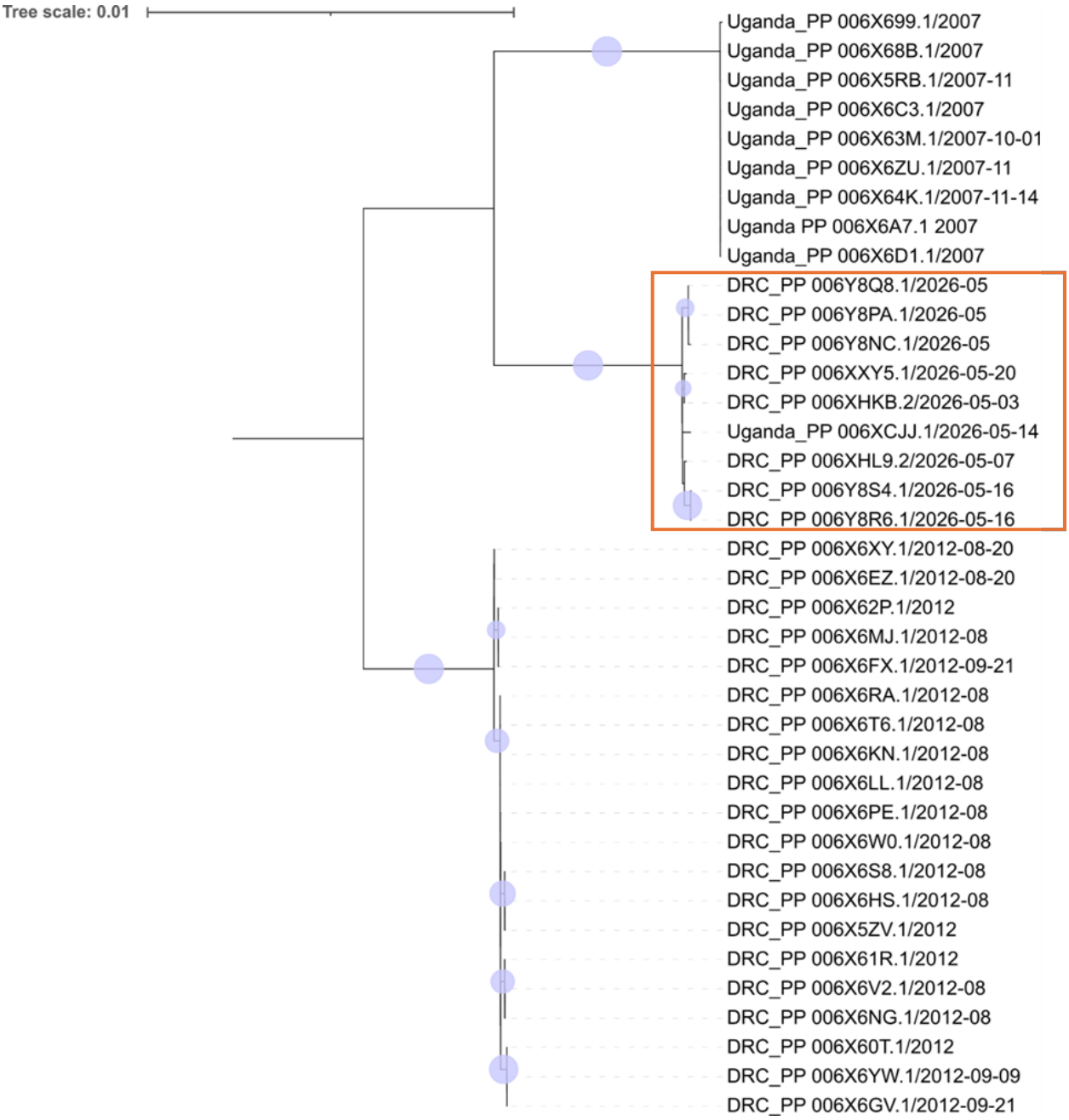
The 2026 genomes so far form a tight phylogenetic cluster with low genetic divergence between sequences (Figure 1) with estimates of initial infection occurring a month prior.[2]

The ongoing 2026 outbreak has been declared a Public Health Emergency of International Concern (PHEIC) by the WHO and the scale and spread of the current outbreak is greater than previous *Orthoebolavirus* outbreaks. [8,14] Table 1 summarizes nonsynonymous substitutions identified in BDBV genomes from the 2012 Isiro outbreak and recent 2026 outbreak genomes.

In brief, persistent nonsynonymous substitutions shared between the 2012 Isiro outbreak and recent 2026 genomes were concentrated predominantly within the GP gene, particularly within the GP1 and mucin-like domains (MLD), suggesting evolutionary maintenance of variation in antigenically exposed regions of the viral surface glycoprotein. Several substitutions are noted, including GP:P365S, GP:P367L, GP:P389L, and GP:R394G, localized to the MLD, a region implicated in immune shielding and antibody accessibility in ebolaviruses. Additional substitutions, including GP:Y151F and GP:E188K, occur near receptor-associated GP1 regions and may warrant future structural or functional investigation. No shared substitutions were observed between the 2007 and 2026 BVD outbreaks.

Newly observed substitutions in the 2026 genomes, including GP:R506S and polymerase-associated substitutions within the L gene, may represent emerging lineage-specific variation; however, no experimental evidence currently supports altered viral fitness, transmissibility, or pathogenicity associated with these variants.[15,16]

Figure 1: Maximum-likelihood Phylogenetic Tree of BDBV Genomic Sequences from 2007, 2012, and 2026 (current) Outbreaks



Notes: The tree was constructed in IQ-Tree2[17] and visualised using ITOL[18]. Circles at nodes indicate bootstrap support values of ≥ 80% with larger circles indicated greater support. Sequences from the ongoing 2026 outbreak are indicated with the orange box.

Table 1: Non-synonymous Substitutions Identified in BDBV Genomes from the 2012 DRC (Isiro) and Recent 2026 Outbreaks through Comparative Genomic Analysis

Gene: Mutation	Genome SNP position(s)	2012 Isiro outbreak	2026 outbreak
GP:Y151F	6472:A>T	Yes	Yes
GP:E188K	6582:G>A; 6584:A>G	Yes	Yes
GP:P365S	7112:C>T	Yes	Yes
GP:P367L	7118:C>T; 7119:C>T; 7120:A>G	Yes	Yes
GP:P389L	7185:C>T	Yes	Yes
GP:R394G	7199:A>G	Yes	Yes
GP:T458I	7392:C>T	Yes	Yes
GP:P481L	7461:C>T	Yes	Yes
GP:T486I	7476:C>T	Yes	Yes
GP:A489V	7485:C>T	Yes	Yes
GP:Y213H	6657:T>C	No	Yes
GP:P344S	7049:C>T	No	Yes
GP:R506S	7537:A>C	No	Yes
VP30:H5Y	8508:C>T	No	Yes
L:K1738N	16780:A>C	No	Yes
L:Q1770R	16875:A>G	No	Yes

Notes: Amino acid numbering is based on the full translated coding sequence (CDS) of the Bundibugyo virus reference genome FJ217161.1. Functional interpretations are inferred primarily from comparative genomics. [15,16]

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