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Decoding Filoviridae: The Molecular Mechanics of Ebola, Marburg, and Beyond

Biology * Public Health * DNA

Phylogeny and Modern Taxonomy of Filoviridae

The family Filoviridae (order Mononegavirales) comprises enveloped, negative-sense, single-stranded RNA viruses causing severe hemorrhagic fevers in humans and primates, notably the 2014-2016 West African Ebola epidemic and the 2026 Bundibugyo virus Public Health Emergency of International Concern (PHEIC) centered in the Democratic Republic of the Congo (DRC)[1][2][3][7]. Under 2025-2026 Master Species List updates (MSL40/MSL41) ratified by the International Committee on Taxonomy of Viruses (ICTV), filovirus taxonomy spans mammalian, piscine, and reptilian hosts[7][8][9]. While Orthoebolavirus and Orthomarburgvirus drive major public health emergencies, bat-borne Cuevavirus (Lloviu virus) and Dianlovirus reflect wide Eurasian chiropteran diversity without causing severe disease in interferon-knockout mice[9][10][11].

| Genus | | Representative Species | | Virus Name (Abbreviation) | | Primary Known Host/Reservoir | | Human Pathogenicity |

| Orthoebolavirus | | O. zairense | | Ebola virus (EBOV) | | Bats (suspected), Primates | | Extremely High |

| Orthoebolavirus | | O. sudanense | | Sudan virus (SUDV) | | Unknown | | High |

| Orthoebolavirus | | O. bundibugyoense | | Bundibugyo virus (BDBV) | | Unknown | | High |

| Orthoebolavirus | | O. restonense | | Reston virus (RESTV) | | Macaques, Domestic Pigs | | Apathogenic |

| Orthoebolavirus | | O. bombaliense | | Bombali virus (BOMV) | | Free-tailed bats | | Likely Low |

| Orthoebolavirus | | O. taiense | | Ta Forest virus (TAFV) | | Unknown | | High |

| Orthomarburgvirus | | O. marburgense | | Marburg / Ravn virus (MARV/RAVV) | | Egyptian fruit bats | | Extremely High |

| Cuevavirus | | C. lloviuense | | Lloviu virus (LLOV) | | Schreiber's bats | | Unobserved |

| Dianlovirus | | D. menglaense | | Mengla virus (MLAV) | | Bats | | Unknown |

| Striavirus / Thamnovirus | | S. antennarii / T. percae | | Xilang / Fiwi virus | | Fish | | Non-mammalian |

| Tapjovirus | | T. bothropis | | Tapajos virus (TAPV) | | Reptiles | | Non-mammalian |

Virion Architecture, Helical Nucleocapsids, and Transcriptional Gradients

Measuring ~80 nm in diameter within a host lipid bilayer, the filovirion packages a 13.1-20.9 kb linear RNA genome lacking a 5' cap or 3' poly-A tail[7][12]. Cryo-electron tomography shows nucleoprotein (NP) encapsidating RNA into a left-handed helix stiffened and regulated by VP24 and VP35 proteins[13][14]. Because the viral RNA-dependent RNA polymerase initiates transcription at the 3' promoter and attenuates across intergenic junctions along 3'-NP-VP35-VP40-GP-VP30-VP24-L-5', structural NP is transcribed in vast excess over the 5'-distal L polymerase[7][15].

Molecular Life Cycle: NPC1 Entry, GP Editing, VP40 Plasticity, and VP24/VP30 Regulation

Trimeric surface glycoprotein (GP), shielded from antibodies by N- and O-linked glycosylation, binds C-type lectins, TIM-1, and TAM kinases to trigger macropinocytosis[12][16][17][18]. In acidic late endosomes, cathepsin B and L proteases remove the glycan cap, exposing GP1 to bind Niemann-Pick C1 (NPC1); GP2 then collapses into a six-helix bundle to fuse membranes and release the nucleocapsid into the cytoplasm[12][19][20][21].

Unlike Marburg virus, Orthoebolavirus and Cuevavirus mitigate GP cytotoxicity in the endoplasmic reticulum via co-transcriptional RNA editing: the viral RNA polymerase predominantly synthesizes unedited antibody-decoy sGP (~70-80%) but stutters at a hepta-uridine tract (~20-30%) to insert an extra adenosine into messenger RNA, frameshifting translation to full-length spike GP[22][23][24]. Matrix protein VP40 exhibits structural plasticity -- folding as a trafficking butterfly dimer, a membrane-budding hexamer, or an RNA-binding octameric ring triggered by guanine/adenine-rich host mRNA[25][26][27][28]. Dynamic VP30 phosphorylation at Ser29 (balanced by host PP2A-B56 dephosphorylation recruited by NP) switches the polymerase from transcription to replication[29][30][31], while Ebola VP24 competitively binds karyopherin 5 (KPNA5) to block phosphorylated STAT1 nuclear import and silence interferon signaling[32][33].

Zoonotic Epidemiology, SEIR Dynamics, and Historical Outbreaks

Spilling over from Egyptian fruit bats (Rousettus aegyptiacus) or bushmeat intermediates, filoviruses transmit via infected bodily fluids, unsterilized needles, and post-mortem funeral contact[34][38]. In SEIR epidemiology rooted in Kermack-McKendrick theory, the Ebola basic reproduction number (R0) averages 1.3-2.0 (1.83 in 1995 Kikwit; 1.34 in 2000 Uganda), with nosocomial superspreading reaching 5-10[35][36][37].

| Year | | Location | | Virus Species | | Cases | | Deaths | | CFR (%) | | Source |

| 1967 | | Germany/Yugoslavia | | Marburg virus | | 31 | | 7 | | 23% | | [34][40] |

| 1976 | | Zaire (DRC) | | Ebola virus | | 318 | | 280 | | 88% | | [38][39] |

| 1995 | | DRC | | Ebola virus | | 315 | | 250 | | 79% | | [35][38] |

| 2000 | | Uganda | | Sudan virus | | 425 | | 224 | | 53% | | [36][38] |

| 2004-05 | | Angola | | Marburg virus | | 252 | | 227 | | 90% | | [34] |

| 2014-16 | | West Africa (Multi) | | Ebola virus | | ~28,600 | | ~11,323 | | ~40-60% | | [38][39] |

| 2023 | | Equatorial Guinea | | Marburg virus | | 16 | | 12* | | 75% | | [34] |

| 2024 | | Rwanda | | Marburg virus | | 66 | | 15 | | 23% | | [34] |

| 2026 | | DRC (+ regional/EU spillovers; Uganda ended Aug 27) | | Bundibugyo virus | | 11,376 (DRC as of Nov 14) | | 5,568 (DRC) | | ~48.9% | | [1][3][5] |

Landmark outbreaks span the 1967 Marburg discovery from imported Ugandan monkeys (Cercopithecus aethiops)[40]; the 1976 Yambuku Zaire (88% CFR, characterized with Peter Piot and international teams) and Nzara Sudan epidemics[38][39]; the 2014-2016 West African epidemic (>28,600 cases, >11,300 deaths)[38][39]; and the unprecedented 2026 Bundibugyo virus epidemic.[1][6] Confirmed in May 2026 in the DRC's Ituri Province and initially crossing into Uganda (where 20 confirmed cases and 2 deaths occurred before Uganda declared its outbreak over on August 27, 2026), transmission accelerated across eight DRC provinces -- Ituri, Nord-Kivu, Sud-Kivu, Tshopo, Haut-U l , Bas-U l , Sud-Ubangi, and Nord-Ubangi -- reaching 11,376 confirmed cases and 5,568 deaths (~48.9% CFR) by November 14, 2026, alongside October 2026 spillovers into Kenya (9 cases, 2 deaths, contacts cleared), Nigeria (1 imported case evacuated to Switzerland), and 4 EU/EEA medical evacuations[1][2][3][4][5].

Clinical Pathology, Vaccines, Monoclonal Cocktails, and EUL Diagnostics

After a 2-21 day incubation, fever and myalgia progress to gastrointestinal fluid loss, endothelial and hepatic injury, coagulopathy, multiorgan failure around days 8-9, or persistence in immune-privileged sites[34][41]. While single-dose rVSV-ZEBOV Ervebo (FDA-approved 2019; following May 2026 EU withdrawal of Zabdeno/Mvabea) and monoclonal therapies Inmazeb and Ebanga transformed Zaire ebolavirus care, they lack licensed efficacy against BDBV -- spurring evaluation of cross-reactive maftivimab and the July 2, 2026 WHO Emergency Use Listing of the first rapid BDBV diagnostic assay[42][43][44][45].

Conclusion: Conserved Targets for Pan-Filovirus Preparedness

Filoviruses achieve high lethality via GP RNA editing, VP40 conformational switching, VP30 phosphorylation toggles, and VP24-KPNA5 immune blockade. Containing the expanding 2026 Bundibugyo crisis requires pan-filovirus vaccines, broad-spectrum therapeutics targeting conserved NPC1 and polymerase domains, and decentralized diagnostics.[1][44]

Updates... (Nov 22, 2026): Updated 2026 Bundibugyo virus surveillance figures through mid-November 2026 (11,376 DRC cases and 5,568 deaths across eight provinces, Uganda outbreak conclusion on August 27, 2026, October 2026 spillovers in Kenya and Nigeria, and EU/EEA medical evacuations); fixed typographical formatting on KPNA5 (5); replaced Wikipedia, ResearchGate, PMC/PubMed, bioRxiv, 403, and commercial URLs with verified primary journal DOIs, ICTV, WHO, ECDC, CDC, UKHSA, EMA, and RCSB PDB sources; and standardized verified publication and annotation dates (including UniProtKB O11457 updated Nov 4, 2026) across all 45 Works Cited entries.

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