

The International Committee on Taxonomy of Viruses

Taxonomy Proposal Form, 2024

**Part 1a: Details of taxonomy proposals**

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| **Title:** | Create new family, ‘Usuviridae’, with two genera in the order *Methanobavirales* (class *Caudoviricetes*) | |
| **Code assigned:** | 2024.006A.N.v1.Usuviridae\_newfam |

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| **Author(s), affiliation and email address(es):** | | | |
| **Name** | **Affiliation** | **Email address** | **Corresponding author(s)** X |
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**Part 1b: Taxonomy Proposal Submission**

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| **ICTV Subcommittee:** | | | |
| Animal DNA Viruses and Retroviruses |  | Bacterial viruses |  |
| Animal minus-strand and dsRNA viruses |  | Fungal and protist viruses |  |
| Animal positive-strand RNA viruses |  | Plant viruses |  |
| Archaeal viruses | **X** | General - |  |

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| **List the ICTV Study Group(s) that have seen or have been involved in creating this proposal:** |
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| **Optional – complete only if formally voted on by an ICTV Study Group:** | | | |
| **Study Group** | **Number of members** | | |
| **Votes in support** | **Votes against** | **No vote** |
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| **Submission date:** | 21/06/2024 |

**Part 1c: Feedback from ICTV Executive Committee (EC) meeting**

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| **Executive Committee Meeting Decision code:** | **X** |
| A – Accept |  |
| Ac – Accept subject to revision by relevant subcommittee chair. No further vote required |  |
| U – Accept without revision but with re-evaluation and email vote by the EC |  |
| Uc – Accept subject to revision and re-evaluation and email vote by the EC | **X** |
| Ud – Deferred to the next EC meeting, with an invitation to revise based on EC comments |  |
| J - Reject |  |
| W - Withdrawn |  |

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| **Comments from the Executive Committee:** |
| The GenBank accession number should become public before the online EC vote. |

**Part 1d: Revised Taxonomy Proposal Submission**

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| **Response of proposer:** |
| Both GenBank accession numbers (PP537965 and BK068243) for the viruses classified in this proposal are now public. |

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| **Revision date:** | 11/09/2024 |

**Part 3:** **TAXONOMIC PROPOSAL**

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| **Name of accompanying Excel module:** |
| 2024.006A.N.v1.Usuviridae\_newfam.xlsx |

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| **Taxonomic changes proposed:** | | | |
| Establish new taxon | **X** | Split taxon |  |
| Abolish taxon |  | Merge taxon |  |
| Move taxon |  | Promote taxon |  |
| Rename taxon |  | Demote taxon |  |
| Move and rename |  |

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| **Is any taxon name used here derived from that of a living person:** | | **N** |
| **Taxon name** | **Person from whom the name is derived** | **Attached X** |
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| **Abstract of Taxonomy Proposal:** |
| *Taxonomic rank(s) affected*:  *Duplodnaviria*, *Heunggongvirae*, *Uroviricota*, *Caudoviricetes*, *Methanobavirales*  *Description of current taxonomy*:  Order *Methanobavirales* (class *Caudoviricetes*)currently includes 5 families of viruses infecting methanogenic archaea.  *Proposed* *taxonomic change(s)*:  Create a new family, ‘Usuviridae’ with two genera for classification of viruses infecting human and animal gut associated methanogenic archaea, and include this family into the existing order *Methanobavirales*.  *Justification*:  Whole-proteome-based phylogenomic analysis using VipTree placed MSTV1-like viruses in a distinct clade, outside of the recently established families of tailed viruses associated with methanogenic archaea or other archaeal hosts. |

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| * **Text of Taxonomy proposal:** |
| *Taxonomic rank(s) affected*:  *Duplodnaviria*, *Heunggongvirae*, *Uroviricota*, *Caudoviricetes*, *Methanobavirales*  *Description of current taxonomy*:  Order *Methanobavirales* (class *Caudoviricetes*)currently includes 5 families of viruses infecting methanogenic archaea.  *Proposed* *taxonomic change(s)*:  Create a new family, ‘Usuviridae’ with two genera for classification of viruses infecting human and animal gut associated methanogenic archaea, and include this family into the existing order *Methanobavirales*.  *Demarcation criteria:*  We propose using 95% sequence identity as a species demarcation threshold, to be consistent with the classification of other bacterial and archaeal viruses in the class *Caudoviricetes*.  *Justification*:  *Methanobrevibacter smithii* PS, the dominant human gut methanogenic archaeon, carries a provirus related to tailed bacterial and archaeal viruses of the class *Caudoviricetes* (Krupovic et al., 2010). Recently, it has been shown that the provirus is active and spontaneously reactivated in a small subpopulation of cells to release the virus, named Methanobrevibacter smithii tailed virus 1 (MSTV1). The MSTV1 virions were observed by negative stain transmission electron microscopy outside of the cells and by electron cryo-tomography inside the cells. The virions have a siphovirus-like morphology, with an isometric capsid of ~65 nm in diameter and a long, flexible, non-contractile tail of ~270 nm in length (Fig. 1; Baquero et al., 2024).  Searches in a catalogue of 1,167 genomes from the human gastrointestinal tract (GIT) archaeome database revealed that MSTV1 is present in 20% of all available *M. smithii* genomes (n=465). Given that *M. smithii* is the most prevalent archaeal species in the human GIT, MSTV1 might be one of the main human-associated archaeal viruses. To gain further insights into the diversity and distribution of MSTV1-like viruses, we explored the recently assembled database of 282 high-quality genomes of (pro)viruses associated with methanogenic archaea discovered in silico (Medvedeva et al., 2023). We identified nine complete and nearly complete MSTV1-like virus genomes sharing <95% average nucleotide identity (ANI) and thus representing different virus species. Four of the viruses were found in the human GIT metagenomes, and the other five were detected as proviruses in the GIT metagenomes of diverse animals, including cows, goats, gorillas and pigs. The predicted hosts of the nine MSTV1-like viruses belong to the order Methanobacteriales.  Whole-proteome-based phylogenomic analysis using VipTree placed MSTV1-like viruses in a distinct clade, outside of the recently established families of tailed viruses associated with methanogenic archaea or other archaeal hosts (Fig. 2). Therefore, we propose to classify MSTV1 and related viruses into a new virus family, named ‘Usuviridae’. Among existing family, ‘Usuviridae’ clusters with members of the *Anaerodiviridae* (Fig. 2). Thus, we propose including ‘Usuviridae’ into the existing order *Methanobavirales*.  The genomes of ‘usuvirids’ can be divided into two regions, a conserved part including the structural genes and a hypervariable region including an array of small genes likely implicated in various aspects of virus-host interactions (Fig. 3). The structural module of MSTV1-like viruses includes genes for the hallmark proteins conserved in bacterial and archaeal viruses of the class *Caudoviricetes*, namely, the HK97-like major capsid protein (MCP), portal protein, large subunit of the terminase (TerL) and several tail components (Fig. 3).  The ‘*Usuviridae*’ clade splits into human- and animal-associated subclades (Fig. 2). Viruses from the two subclades display distinct neck-tail modules, with the corresponding proteins showing low or no sequence similarity (Fig. 3). Notably, animal GIT-associated viruses vir406, vir075 and vir128 encode a distinct TerL variant (Fig. 3). Phylogenetic analysis of TerL from tailed viruses infecting environmental and host-associated methanogens revealed that TerL proteins of the three viruses fall into a different clade than the other MSTV1-like viruses (Fig. 4), indicating non-orthologous gene replacement and recombination between different groups of viruses of methanogens, likely facilitated by shared environment and host range. Finally, the human and animal GIT-associated viruses differ in their endolysins implicated in digestion of the archaeal cell wall during virion egress at the end of the infection cycle. Whereas MSTV1 and other human-associated ‘usuvirids’ encode PeiW-like endolysins (Peptidase\_C71 family; Fig. 3), ‘usuvirids’ recovered from the animal GIT encode PeiR-like endolysins (Peptidase\_C39 family; Fig. 3). These differences between human and animal GIT-associated ‘usuvirids’ likely reflect distinct adaptations to the respective hosts and ecological contexts. Thus, we propose to classify the ‘usuvirids’ associated with the human and animal gut associated archaea into distinct genera, ‘Manusuvirus’ and ‘Hewusuvirus’, respectively.  Only two of the MSTV1-like virus genomes could be submitted to GenBank. Thus, only two species, ‘Manusuvirus methanobrevibacteri’ and ‘Hewusuvirus methanobrevibacteri’, will be created at this point in the genera ‘Manusuvirus’ and ‘Hewusuvirus’, respectively.  **Etymology:**  ‘Usuviridae’, after ‘usus’, intestine in Indonesian.  ‘Manusuvirus’, after ‘manusia’, human in Indonesian  ‘Hewusuvirus’, after ‘hewan’, animal in Indonesian.  ‘*methanobrevibacteri*’, after the host genus name, *Methanobrevibacter*. |

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| **References:** |
| Baquero DP, Medvedeva S, Martin-Gallausiaux C, Pende N, Sartori-Rupp A, Tachon S, Pedron T, Debarbieux L, Borrel G, Gribaldo S, Krupovic M. Stable coexistence between an archaeal virus and the dominant methanogen of the human gut. Nat Commun. 2024 Sep 4;15(1):7702. doi: 10.1038/s41467-024-51946-x.  Krupovic M, Forterre P, Bamford DH. Comparative analysis of the mosaic genomes of tailed archaeal viruses and proviruses suggests common themes for virion architecture and assembly with tailed viruses of bacteria. J Mol Biol. 2010; 397(1):144-60. doi: 10.1016/j.jmb.2010.01.037. PMID: 20109464  Medvedeva S, Borrel G, Krupovic M, Gribaldo S. A compendium of viruses from methanogenic archaea reveals their diversity and adaptations to the gut environment. Nat Microbiol. 2023; 8(11):2170-2182. doi: 10.1038/s41564-023-01485-w. PMID: 37749252  Nguyen LT, Schmidt HA, von Haeseler A, Minh BQ. IQ-TREE: a fast and effective stochastic algorithm for estimating maximum-likelihood phylogenies. Mol Biol Evol. 2015; 32(1):268-74. doi: 10.1093/molbev/msu300. PMID: 25371430 |

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| **Tables, Figures:** |

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Close-up of a microscopic view of a cell

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Figure 1. Transmission electron micrographs of MSTV1 virions. The top image displays an MSTV1 virion attached to the *M. smithii* surface. Scale bar, 200 nm. The bottom image shows MSTV1 virion found in the supernatant of *M. smithii* cultures. Scale bar, 100 nm.

A diagram of a number of people

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Figure 2. Proteomic tree of head-tailed viruses infecting methanogenic and hyperhalophilic archaea. Families of viruses associated with methanogenic archaea are highlighted with colored background. Branch lengths are log-scaled and the branch length for family-level demarcation is around 0.05. MSTV1 is indicated in bold within the newly proposed virus family ‘Usuviridae’.

A diagram of arrows and lines

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Figure 3. Alignment of MSTV1-like viruses originating from human and animal GIT. ORFs are depicted by arrows that indicate the direction of transcription. Functional annotations are shown above the corresponding ORFs. Homologous genes are depicted with the same colors and are connected by shading in grayscale, with intensity reflecting the amino acid sequence identity. Cdc6: AAA+ ATPase Orc1/Cdc6; HEPN: higher eukaryotes and prokaryotes nucleotide-binding domain-containing protein; int: integrase; MCP: major capsid protein; mCP: minor capsid protein; MTase: methyltransferase; NTN-hydrolase: N‐terminal nucleophile hydrolase; Prot: serine protease; RHH: ribbon-helix-helix protein; TAC: tail assembly chaperone; TerL: terminase large subunit; TerS: terminase small subunit; TMP: tail tape measure protein; TTP: tail tube protein; wHTH: winged helix-turn-helix domain; ZF: zinc finger domain-containing protein.

A diagram of a tree

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Figure 4. Phylogenetic analysis of TerL proteins encoded by viruses related to Methanobacteriales. MSTV1-like viruses are depicted in blue. The maximum likelihood phylogeny was inferred using IQTree (best model Q.pfam+F+I+R4) (Nguyen et al., 2015). Scale bar represents the number of substitutions per site.