This Word module should be used for all taxonomic proposals.

Please complete **Part 1** and:

either **Part 3** for proposals to create new taxa or change existing taxa

or **Part 2** for proposals of a general nature.

Submit the completed Word module, together with the accompanying Excel module named in Part 3, to the appropriate ICTV Subcommittee Chair.

For guidance, see the notes written in blue, below, and the help notes in file Taxonomic\_Proposals\_Help\_2018.

**Part 1:** **TITLE, AUTHORS, etc**

|  |  |  |
| --- | --- | --- |
| **Code assigned:** |  | (to be completed by ICTV officers) |
| **Short title:** (e.g. “6 new species in the genus *Zetavirus”*)18 new species in the family *Herpesviridae* |
|  |
| **Author(s):** |
| Members of the *Herpesvirales* study group:Gatherer, DerekBenkő, MáriaBrandt, CurtisBryant, NeilDastjerdi, AkbarDepledge, DanielDoszpoly, AndorGompels, UrsulaHartley, CarolInoue, NaokiJarosinski, Keith Kaul, RajeevLacoste, VincentNorberg, PeterOriggi, FrancescoOrton, RichardPellett, PhilipSchmid, ScottStewart, JamesSzpara, MoriahTrimpert, JakobVaz, PaolaWaltzek, TomDavison, AndrewOthers who provided unpublished information:Beatty, JuliaJarvis, MichaelMiller, MyrnaTroyer, Ryan |

|  |
| --- |
| **Corresponding author with e-mail address:** |
| Andrew Davison (andrew.davison@glasgow.ac.uk) |
| **List the ICTV study group(s) that have seen this proposal:** |
| A list of study groups and contacts is provided at <http://www.ictvonline.org/subcommittees.asp> . If in doubt, contact the appropriate subcommittee chair (there are six virus subcommittees: animal DNA and retroviruses, animal ssRNA-, animal ssRNA+, fungal and protist, plant, bacterial and archaeal) | ***Herpesvirales*** |
| **ICTV Study Group comments (if any) and response of the proposer:** |
|       |
|  |
| Date first submitted to ICTV: |       |
| Date of this revision (if different to above): |       |
| **ICTV-EC comments and response of the proposer:** |
|       |

**Part 3:** **PROPOSED TAXONOMY**

|  |
| --- |
| Name of accompanying Excel module: Herpesvirales\_2018.xlsx |

The taxonomic changes you are proposing should be presented on an accompanying Excel module, 2017\_TP\_Template\_Excel\_module. Please enter the file name of the completed module in this box.

**Supporting material:**

| additional material in support of this proposal |
| --- |
| Please explain the reasons for the taxonomic changes you are proposing and provide evidence to support them. The following information should be provided, where relevant:* **Species demarcation criteria**: Explain how new species differ from others in the genus and demonstrate that these differences meet the criteria previously established for demarcating between species. If no criteriahave previously been established, and if there will now be more than one species in the genus, please state the demarcation criteria you are proposing.
* **Higher taxa**:
	+ There is no formal requirement to state demarcation criteria when proposing new genera or other higher taxa. However, a similar concept should apply in pursuit of a rational and consistent virus taxonomy.
	+ Please indicate the **origin of names** assigned to new taxa at genus level and above.
	+ For each new genus a **type species** must be designated to represent it. Please explain your choice.
* **Supporting evidence**: The use of Figures and Tables is strongly recommended (note that copying from publications will require permission from the copyright holder). For phylogenetic analysis, try to provide a tree where branch length is related to genetic distance.
 |

**Introduction**

# Genome sequences are available for a sizeable number of herpesviruses that need to be classified. The *Herpesvirales* Study Group plans to approach this in a staged fashion. This year, we focus on the family *Herpesviridae* and propose the classification of 18 new species in existing genera and the placement of one existing species, which was not assigned to a genus, into an existing genus.

# Species demarcation criteria

# The species demarcation criteria for the order *Herpesvirales* are outlined in the 9th ICTV Report: “A herpesvirus may be classified as a species if it has distinct epidemiological or biological characteristics and a distinct genome that represents an independent replicating lineage. Sequence information is required for formal recognition of new herpesvirus species. Replicating lineages of herpesviruses are now identified primarily on the basis of information derived from genomic sequences. Sequence information sufficient to demonstrate that a novel virus represents a replicating lineage distinct from known herpesvirus species is taken as evidence that the virus in question exists in nature, occupies a distinct ecological niche and thus can be recognized as a herpesvirus species. For some well-studied genes, there are levels of sequence difference beyond which there are no instances in which the viruses in question do not have distinct epidemiological and biological properties; such viruses can be reliably recognized as species on the basis of limited sequence information. There are also closely related viruses that have relatively small differences in the sequences of individual genes, but genetic differences extend across the respective genomes in a manner indicative of them representing independent replicating lineages. These viruses also have distinct epidemiological and biological characteristics (e.g. host identity, pathogenic and epidemiological properties, and the lack of occurrence of natural recombinants) and thus meet the definition of herpesvirus species.”

The dominant factor in herpesvirus classification is sequence-based phylogeny. For such analyses, the Study Group does not mandate complete genome sequences, does not set a dependence on any particular gene or group of genes, or even that the sequence of any particular gene should be complete, and does not specify genetic distance thresholds for differentiating taxa. The rule-of-thumb applied in the proposals below is that the evolutionary distance between each virus to be classified and its closest classified relative should be more than that between the most closely related viruses that have already been classified into the family *Herpesviridae*. Thus, using EMBOSS Distmat (Jukes-Cantor method) to calculate the distances of the concatenated sequences of the genes described below, the previously classified viruses BoAHV5 and BuAHV1 differ by 2.92%, HuBHV6A and HuBHV6B by 3.53%, and EqAHV8 and EqAHV9 by 4.89%. The two viruses proposed for classification that have the nearest previously classified neighbours are McGHV10 (4.40% distant from McGHV4), and McGHV11 (5.08% distant from McGHV5), and thus fit this requirement. Moreover, with two exceptions, the viruses proposed for classification originated from host species different from their nearest neighbours. The exceptions are ElBHV4 and ElBHV5, which infect the same host species as the previously classified ElBHV1. The differential factors for these viruses in addition to evolutionary distance (e.g. 27.25% for ElBHV5 and ElBHV1) are that ElBHV4 has a different nucleotide composition (61% G+C for the six genes analysed) from ElBHV5 and ElBHV1 (both 43% G+C), and that each virus possesses a subset of unique genes.

**Phylogenetic analysis**

Perhaps the most influential phylogenetic studies were carried out in Duncan McGeoch’s group many years ago. These utilised several well conserved genes singly and as concatenations (1-4). Much more sequence information now exists, and, in an attempt to maintain this quality level, we started by deriving the encoded amino acid sequences of 36 genes that have orthologues in 17 viruses representing the known diversity of the family *Herpesviridae*. As in published studies, this required analyses to be carried out at the level of amino acid, rather than nucleotide, sequence. For phylogenetic analysis, we chose to base further comparisons on the encoded amino acid sequences of six generally large, well-conserved genes that produced reliable results. These genes encode uracil-DNA glycosylase, helicase-primase helicase subunit, DNA packaging terminase subunit 1, major capsid protein, envelope glycoprotein B and DNA polymerase catalytic subunit.

We then compiled a comprehensive list of herpesviruses for which the complete sequence of at least one of these genes was available in published form or as unpublished data kindly provided by one or other of the authors of these proposals, and derived the amino acid sequences. This dataset forms a primary resource for these proposals and will also serve in future. For this year, we focused on viruses for which the complete sequences of all six genes were available. A concatenated amino acid sequence alignment was created using Protein Align in MOE (https://www.chemcomp.com/), and phylogenetic trees were constructed in MEGA (5). A neighbour-joining phylogenetic tree (6) using *p*-distances (7) was constructed for use as an initial framework. A heuristic search was then performed using the maximum likelihood method with 100 bootstrap replicates (8) to assess clade confidence.

The three unrooted trees shown below concern viruses that group into subfamilies *Alphaherpesvirinae*, *Betaherpesvirinae* and *Gammaherpesvirinae* of family *Herpesviridae*. The connection of these subfamilies in the family has been demonstrated frequently, amply and stably in the literature (2) and is not reproduced here. The names of the existing genera into which the viruses fall are shown on the right. Bootstrap values of 70 or more are also shown. The apparent root of an unrooted tree is a presentational artefact and does not carry a bootstrap value.

A herpesvirus species name consists of three elements. The first is derived from a taxon of the host that in its natural setting harbors the virus. The default taxon employed is that of family, and, except for the species of humans, it ends in ‘-id’. Exceptions are viral species from the family Bovidae, which are designated by host subfamily or genus, and nonhuman primates (host genus); these names end in ‘-ine’. The second element is the word ‘alphaherpesvirus’, ‘betaherpesvirus’ or ‘gammaherpesvirus’, depending on the subfamily to which the virus belongs. The third element is a numeral, in two cases followed by a letter. It is important to register that the numeral is intended solely to provide an unique identifier. It does not imply the existence of a complete or continuous series, or any particular relationship between viruses in difference series that carry the same numeral, and is chosen as much as is possible to avoid confusion in relation to the numerals used in virus names in the literature. Thus, for example, there is currently a single elephant herpesvirus species (*Elephantid betaherpesvirus 1*), and the two proposed species are *Elephantid betaherpesvirus 4* and *Elephantid betaherpesvirus 5* because the viruses have been designated in the literature as elephant endotheliotropic herpesviruses 4 and 5. This leaves the potential names *Elephantid betaherpesvirus 2* and *Elephantid betaherpesvirus 3* currently unassigned.

A virus may have several names in the literature, and these may be used inconstistently. To avoid confusion, the short forms of virus names in this proposal are related to the species names, and commence as follows.

Al alcelaphine

An anatid

Ao aotine

At ateline

Bo bovine

Bu bubaline

Ca canid

Cd caviid

Ce cercopithecine

Ch chelonid

Cl callitrichine

Co columbid

Cr cricetid

Cv cervid

De delphinid

El elephantid

Eq equid

Fe felid

Ga gallid

Hu human

Le leporid

Ma macropodid

Mc macacine

Md mandrilline

Me meleagrid

Mn miniopterid

Mo monodontid

Ms mustelid

Mu murid

Ov ovine

Pa papiine

Ph phocid

Pn panine

Ps psittacid

Pt pteropodid

Sa saimiriine

Sp spheniscid

Su suid

Te testudinid

Tu tupaiid

Ve vespertilionid

These two letters are followed by three more to indicate the subfamily (AHV, *Alphaherpesvirinae*; BHV, *Betaherpesvirinae*; GHV, *Gammaherpesvirinae*), and finally by a numeral (and a further letter in two cases). Thus, the abbreviation corresponds to the existing or proposed species name (e.g. BoAHV5, *Bovine alphaherpesvirus 5*).

The key to the branches in the trees is as follows.

 Already classified; data in tree are published; taxonomic changes are not proposed

 Already classified; data in tree are not published; taxonomic changes are not proposed

 Not classified; data in tree are published; **classification is proposed**

 Not classified; data in tree are published; classification is not proposed

 Already classified into species but not genus; **taxonomic change is proposed**

 Not classified and identities not shown; data in tree are not published; classification is not proposed

**Taxonomic proposals**

The creation of the following species (with virus name abbreviations in parentheses) and their assignment to the relevant genera and subfamilies is supported by our analysis and explicitly by analyses in the following papers reporting the sequence data.

*Pteropodid alphaherpesvirus 1* (PtAHV1) (9)

*Monodontid alphaherpesvirus 1* (MoAHV1) (10)

*Spheniscid alphaherpesvirus 1* (SpAHV1) (11)

*Testudinid alphaherpesvirus 3* (TeAHV3) (12)

*Macacine betaherpesvirus 8* (McBHV8) (13)

*Mandrilline betaherpesvirus 1* (MdBHV1) (14)

*Papiine betaherpesvirus 4* (PaBHV4) (14)

*Macacine betaherpesvirus 9* (McBHV9) (15)

*Murid betaherpesvirus 3* (MuBHV3) (16)

*Elephantid betaherpesvirus 4* (ElBHV4) (17)

*Elephantid betaherpesvirus 5* (ElBHV5) (18)

*Macacine gammaherpesvirus 10* (McGHV10) (19)

*Macacine gammaherpesvirus 8* (McGHV8) (20)

*Macacine gammaherpesvirus 11* (McGHV11) (21)

*Macacine gammaherpesvirus 12* (McGHV12) (22)

*Felid gammaherpesvirus 1* (FeGHV1) (23)

*Phocid gammaherpesvirus 3* (PhGHV3) (no paper reporting the sequence)

*Vespertilionid gammaherpesvirus 1* (VeGHV1) (24).

The species *Suid betaherpesvirus 2* (SuBHV2) (25) already exists but has not been assigned to a genus, and is now proposed as a member of the genus *Roseolovirus*. Further details on these proposals are available in the accompanying spreadsheet. The proposals concerning *Murid betaherpesvirus 3* and *Suid betaherpesvirus 2* were supported by a large majority of Study Group members who responded, and the other proposals by all members who responded.

**References**

1. McGeoch DJ, Cook S. 1994. Molecular phylogeny of the Alphaherpesvirinae subfamily and a proposed evolutionary timescale. J Mol Biol 238:9-22. PMID: 8145260.
2. McGeoch DJ, Cook S, Dolan A, Jamieson FE, Telford EA. 1995. Molecular phylogeny and evolutionary timescale for the family of mammalian herpesviruses. J Mol Biol 247:443-58. PMID: 7714900.
3. McGeoch DJ, Dolan A, Ralph AC. 2000. Toward a comprehensive phylogeny for mammalian and avian herpesviruses. J Virol 74: 10401-6. PMID: 11044084.
4. McGeoch DJ, Gatherer D, Dolan A. 2005. On phylogenetic relationships among major lineages of the Gammaherpesvirinae. J Gen Virol 86:307-16. PMID: 15659749.
5. Kumar S, Stecher G, Tamura K. 2016. MEGA7: Molecular Evolutionary Genetics Analysis version 7.0 for bigger datasets. Mol Biol Evol 33:1870-4. PMID: 27004904.
6. Saitou N, Nei M. 1987. The neighbor-joining method: a new method for reconstructing phylogenetic trees. Mol Biol Evol 4:406-25. PMID: 3447015.
7. Nei M, Kumar S. 2000. Molecular Evolution and Phylogenetics, New York, Oxford University Press.
8. Felsenstein J. 1985. Confidence limits on phylogenies: An approach using the bootstrap. Evolution, 39, 783-91. PMID: 28561359.
9. Sasaki M, Setiyono A, Handharyani E, Kobayashi S, Rahmadani I, Taha S, Adiani S, Subangkit M, Nakamura I, Sawa H, Kimura T. 2014. Isolation and characterization of a novel alphaherpesvirus in fruit bats. J Virol 88:9819-29. PMID: 24942567.
10. Davison AJ, Nielsen O, Subramaniam K, Jacob JM, Romero CH, Burek-Huntington KA, Waltzek TB. 2017. Genome sequence of an alphaherpesvirus from a beluga whale (*Delphinapterus leucas*).Genome Announc 5:e01100-17. PMID: 29051247.
11. Pfaff F, Schulze C, König P, Franzke K, Bock S, Hlinak A, Kämmerling J, Ochs A, Schüle A, Mettenleiter TC, Höper D, Beer M. 2017. A novel alphaherpesvirus associated with fatal diseases in banded penguins. J Gen Virol 98:89-95. PMID: 28036249.
12. Gandar F, Wilkie GS, Gatherer D, Kerr K, Marlier D, Diez M, Marschang RE, Mast J, Dewals BG, Davison AJ, Vanderplasschen AF. 2015. The genome of a tortoise herpesvirus (testudinid herpesvirus 3) has a novel structure and contains a large region that is not required for replication *in vitro* or virulence *in vivo*. J Virol 89:11438-56. PMID: 26339050.
13. Marsh AK, Willer DO, Ambagala AP, Dzamba M, Chan JK, Pilon R, Fournier J, Sandstrom P, Brudno M, MacDonald KS. 2011. Genomic sequencing and characterization of cynomolgus macaque cytomegalovirus. J Virol 85:12995-3009. PMID: 21994460.
14. Blewett EL, Sherrod CJ, Texier JR, Conrad TM, Dittmer DP. 2015. Complete genome sequences of *Mandrillus leucophaeus* and *Papio ursinus* cytomegaloviruses. Genome Announc 3:e00781-15. PMID: 26251484.
15. Staheli JP, Dyen MR, Deutsch GH, Basom RS, Fitzgibbon MP, Lewis P, Barcy S. 2016. Complete unique genome sequence, expression profile, and salivary gland tissue tropism of the herpesvirus 7 homolog in pigtailed macaques. J Virol 90:6657-74. PMID: 27170755.
16. Patel SJ, Zhao G, Penna VR, Park E, Lauron EJ, Harvey IB, Beatty WL, Plougastel-Douglas B, Poursine-Laurent J, Fremont DH, Wang D, Yokoyama WM. 2017. A murine herpesvirus closely related to ubiquitous human herpesviruses causes T-cell depletion. J Virol 91:e02463-16. PMID: 28179532.
17. Ling PD, Long SY, Fuery A, Peng RS, Heaggans SY, Qin X, Worley KC, Dugan S, Hayward GS. 2016. Complete genome sequence of elephant endotheliotropic herpesvirus 4, the first example of a GC-rich branch proboscivirus. mSphere 1:e00081-15. PMID: 27340695.
18. Wilkie GS, Davison AJ, Kerr K, Stidworthy MF, Redrobe S, Steinbach F, Dastjerdi A, Denk D. 2014. First fatality associated with elephant endotheliotropic herpesvirus 5 in an Asian elephant: pathological findings and complete viral genome sequence. Sci Rep. 4:6299. PMID: 25199796.
19. Kamperschroer C, Gosink MM, Kumpf SW, O'Donnell LM, Tartaro KR. 2016. The genomic sequence of lymphocryptovirus from cynomolgus macaque. Virology 488:28-36. PMID: 26590795.
20. Bruce AG, Ryan JT, Thomas MJ, Peng X, Grundhoff A, Tsai CC, Rose TM. 2013. Next-generation sequence analysis of the genome of RFHVMn, the macaque homolog of Kaposi's sarcoma (KS)-associated herpesvirus, from a KS-like tumor of a pig-tailed macaque. J Virol 87:13676-93. PMID: 24109218.
21. Estep RD, Hansen SG, Rogers KS, Axthelm MK, Wong SW. 2013. Genomic characterization of Japanese macaque rhadinovirus, a novel herpesvirus isolated from a nonhuman primate with a spontaneous inflammatory demyelinating disease. J Virol 87:512-23. PMID: 23097433.
22. Bruce AG, Thouless ME, Haines AS, Pallen MJ, Grundhoff A, Rose TM. 2015. Complete genome sequence of pig-tailed macaque rhadinovirus 2 and its evolutionary relationship with rhesus macaque rhadinovirus and human herpesvirus 8/Kaposi's sarcoma-associated herpesvirus. J Virol 89:3888-909. PMID: 25609822.
23. Troyer RM, Lee JS, Vuyisich M, Chain P, Lo CC, Kronmiller B, Bracha S, Avery AC, VandeWoude S. 2015. First complete genome sequence of *Felis catus* gammaherpesvirus 1. Genome Announc 3:e01192-15. PMID: 26543105.
24. Shabman RS, Shrivastava S, Tsibane T, Attie O, Jayaprakash A, Mire CE, Dilley KE, Puri V, Stockwell TB, Geisbert TW, Sachidanandam R, Basler CF. 2016. Isolation and characterization of a novel gammaherpesvirus from a microbat cell line. mSphere 1:e00070-15. PMID: 27303702.
25. Gu W, Zeng N, Zhou L, Ge X, Guo X, Yang H. 2014. Genomic organization and molecular characterization of porcine cytomegalovirus. Virology 460-1:165-72. PMID: 25010282.

**Phylogeny of viruses in subfamily *Alphaherpesvirinae***

**Phylogeny of viruses in subfamily *Betaherpesvirinae*Phylogeny of viruses in subfamily *Gammaherpesvirinae***