

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

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| **Code assigned:** | **2021.001S** |  |
| **Short title:** Create two subfamilies **(***Orthohepevirinae*, *Parahepevirinae*), four genera and five species, and rename five species (*Hepelivirales*: *Hepeviridae*) | | |
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**Corresponding author**

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| Smith, DB (Chair Hepeviridae Study Group) |

**List the ICTV Study Group(s) that have seen this proposal**

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| Hepeviridae SG (author) |

**ICTV study group comments and response of proposer**

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| Voted on by Study group – a majority (8 for, 1 against) were in favour of new taxonomy and genus names. However, there was no clear majority on the format of species names. In addition, some of the species names use the first few letters of the authors of the paper first describing a virus in that species – the SG was unclear if permission would be needed in this case. One name (balayan) derives from a person who has died.  The SG would like to be given time to reach a consensus on the species names after the SCC and EC has given their feedback. |

**Authority to use the name of a living person**

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| **Is any taxon name used here derived from that of a living person (Y/N)** | N |

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| **Taxon name** | **Person from whom the name is derived** | **Permission attached (Y/N)** |
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**Submission dates**

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| Date first submitted to SC Chair |  |
| Date of this revision (if different to above) |  |

**ICTV-EC comments and response of the proposer**

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| *ICTV-EC Comments*  Dear Donald and study group    Many thanks for submitting the proposal for a extensive taxonomy revision and expansion for *Hepeviridae*. This was reviewed at the ICTV Executive Committee meeting and it was given a designation of Ac. This means that it is accepted pending the issue of proposed species names. This was specifically discussed as an agenda item at the EC meeting to seek clarification on whether parts of names (1-3 letters) fell within the scope of rule 3.11 of the ICTV code. The text of this rule is:    A person's name may be used when devising a name for new taxon. If the person is alive at the time of the proposal, the person’s written consent for use of his/her/their name must be provided together with the official taxonomic proposal. Whether the use of a person’s name for taxon naming is appropriate will be judged by the responsible ICTV Study Group, the respective ICTV Subcommittee, and the ICTV Executive Committee and approved or disapproved following established taxonomic proposal procedures. Furthermore, a) An individual may not propose his/her/their own name as the basis for any new taxon name; and b) A taxon may not be named wholly or in part after any current member of an ICTV Study Group or Committee.:    After some discussion, it was considered that parts of names used for species designations remained potentially recognisable and would therefore fall within the scope of rule 3.11. This means that the several proposed names for new species would not be acceptable as many referred to living scientists without permissions being sought. Two were furthermore created from names of SG members, disallowed under Section (b).    We would therefore ask you to review the species names and develop alternatives, in binomial format, that would avoid invoking rule 3.11, or where relevant provide permissions from the relevant scientists for use of their names.  Not discussed at the meeting but another point to consider might be the proposed name of the genus, Pashepevirus. This is going to be the most commonly used genus name but its pronunciation isn’t obvious, would it be pas-hepevirus or pashe-pevirus? I was just wondering whether it could be slightly modified so it’s obvious how to say it? As it contains rabbits (Lagomorpha), how about Praslahepevirus (Pr + A + S + La)?  Otherwise this was an excellent proposal and the promotion of ranks was felt to be highly appropriate and bring hepevirus taxonomy more in line with those of other animal positive strand RNA viruses.  *Response*  In response to comments from the ICTV, the proposed species epithets have been updated so that they no longer include parts of names of living persons. Upon reflection, the SG have decided that they no longer wish to assign the tree shrew hepatitis E virus to a new species; this is because the only sequence available is unsupported by a publication and the definitive host is not stated. |

**Part 2:** **NON-TAXONOMIC PROPOSAL**

**Text of proposal**

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

**Name of accompanying Excel module**

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| 2021.001S.A.v1.Hepeviridae.xlsx |

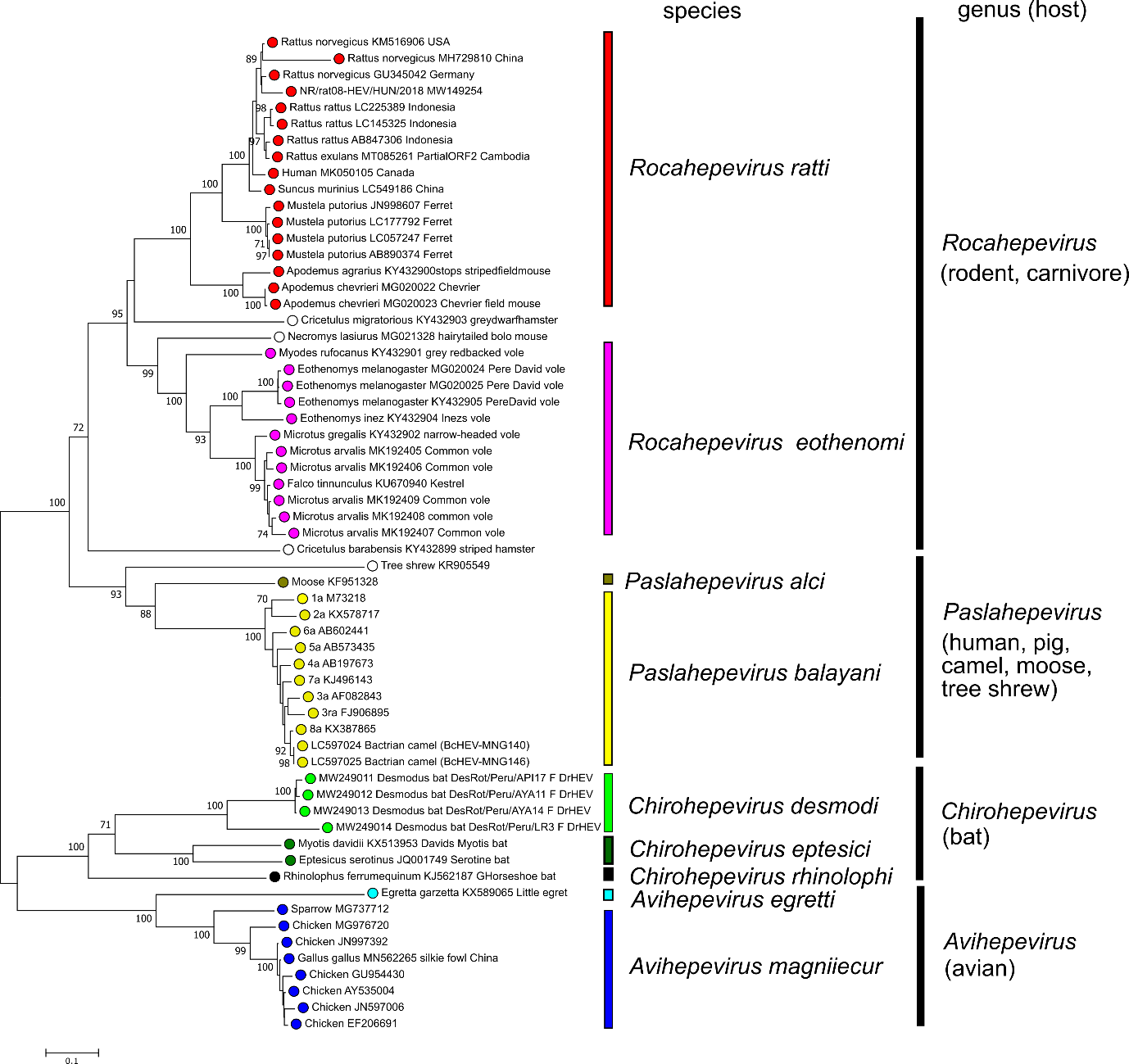
**Abstract**

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| We propose that the family *Hepeviridae* (currently 2 genera and 5 species) be expanded to include 2 subfamilies, 5 genera and 10 species; this reorganization is based on the phylogenetic analysis of three genome regions and host associations. |

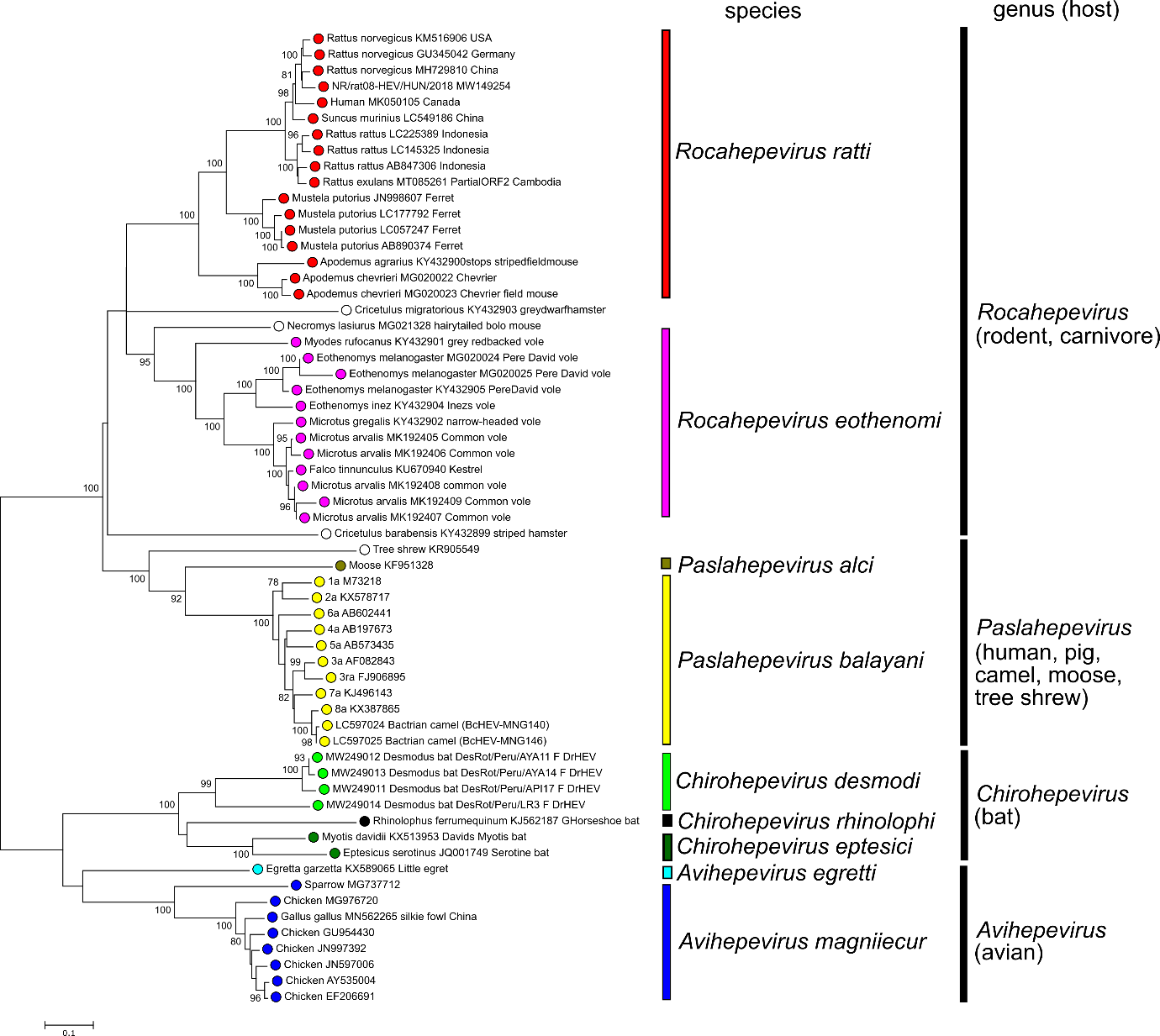
**Text of proposal**

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These viruses fall into five clear host groups, each of which contains members of only one of the current five species:   1. Fish viruses (including members of *Piscihepevirus* *A*) 2. Human, pig, camel, moose and tree shrew viruses (including members of *Orthohepevirus* *A*) 3. Avian viruses (including members of *Orthohepevirus B*) 4. Rodent and carnivore viruses (including members of *Orthohepevirus C*) 5. Bat viruses (including members of *Orthohepevirus D*)   Apart from the (little studied) fish viruses, each of these groups is diverse, this diversity correlating with host species. We have therefore taken the decision to promote the taxa including these five groups from species to genera. The two existing genera are likewise promoted to subfamilies (Table 1).  Table 1 Proposed classification of the family *Hepeviridae*   |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Family** | **Subfamily** | **Genus** | **Species** | **Genotype** | **Reference accession** | **Predominant host** | | *Hepeviridae* | *Orthohepevirinae* | *Paslahepevirus* | *balayani* | HEV-1 | M73218 | Human (*Homo sapiens*) | | HEV-2 | KX578717 | Human | | HEV-3 | AF082843 | Human, pig, wild boar (*Sus scrofa*), deer, rabbit | | HEV-4 | AJ272108 | Human, pig, wild boar | | HEV-5 | AB573435 | Wild boar | | HEV-6 | AB602441 | Wild boar | | HEV-7 | KJ496143 | Dromedary camel (*Camelus dromedarius*) | | HEV-8 | KX387865 | Bactrian camel *(Camelus bactrianus*) | | *alci* |  | KF951328 | Moose (*Alces alces*) | |  |  |  |  | | *Avihepevirus* | *magniiecur* |  | AY535004 | Chicken (*Gallus gallus*), sparrow (*Passer domesticus*) | | *egretti* |  | KX589065 | Little egret (*Egretta garzetta*) | | *Rocahepevirus* | *ratti* | HEV-C1 | GU345042 | Rat (several *Rattus* sp. and *Suncus murinus*) | | HEV-C2 | JN998606 | Ferret (*Mustela putorius*) | |  | HEV-C3 | MG020022 | Field mice (*Apodemus* sp) | | *eothenomi* |  | MG020024 | Vole (various species in tribe Arvicolini) | | *Chirohepevirus* | *eptesici* |  | JQ001749 | Bats (*Eptesicus serotinus*) and (*Myotis davidii*) | | *rhinolophi* |  | KJ562187 | Horseshoe bat (*Rhinolophus ferrumequinum*) | | *desmodi* |  | MW249011 | Bat (*Desmodus rotundus* ) | | *Parahepevirinae* | *Piscihepevirus* | *heenan* |  | HQ731075 | Trout (*Oncorhynchus clarkii*) |   In support of this proposal we present phylogenetic analysis of members of the proposed subfamily *Orthohepevirinae* (viruses in host groups 2 to 5) for three different regions of the virus genome – ORF1 amino acid positions 1−450 (methyltransferase), ORF1 amino acid positions 971-1692 (RNA-directed RNA polymerase) and ORF2 amino acid positions 121−473 (capsid protein not including the region encoded by the overlapping ORF3). Trees were obtained using the JTT model with bootstrap replication. Consistent host-associated groups are obtained for these three regions (Figures 1 to 3) supporting the proposed taxonomy. Similar topologies were obtained using different phylogenetic methods (not shown). Pairwise sequence distances produced overlapping distributions of distances for all three genome regions, meaning that it was not possible to provide genus or species demarcation criteria based on these distances.  We have chosen not to classify two sequences from hamsters (KY432899 and KY432903) or a virus from *Necromys lasiurus* (MG021328) because of their ambiguous placement in the trees. We have also chosen not to assign the tree shrew virus (KR905549) since there is no publication associated with the GenBank accession, and since the definitive host is not stated. Also unclassified are several more distantly related viruses described from metagenomics studies (“hepe-like” viruses) that share a similar genome organization and domain structure; further work is required to decide if they should be placed in the family *Hepeviridae*.  **Subfamilies**  *Orthohepevirinae* – the prefix ortho meaning right, correct  *Parahepevirinae* – the prefix para meaning near  **Genera**  *Paslahepevirus* - Primates, Artiodactyla, Scandentia, Lagomorpha  *Avihepevirus* from Avian  *Rocahepevirus* from Rodentia & Carnivora  *Chirohepevirus*from Chiroptera.  *Piscihepevirus* - unchanged  **Species**  Most species names are Latinised descriptors of the host in which virus in that virus species was first detected. One species epithet (*balayani*) honours a person who is no longer alive, one (*magniiecur*) is a Latinised description of the symptoms produced by virus infection, and one (*heenan*) derives from the place of first isolation.  *Paslahepevirus balayan* for human/pig/camel HEV refers to the first hepatitis E virus paper  Balayan et al, (1983) [1]  *Paslahepevirus alci*from  *Alces alces* the binomial name of the host, moose  [5]  *Avihepvirus magniiecur*- from the Latin for big liver - *magni iecur*  *Avihepevirus egretti* from *Egretta garzetta* the binomial name of the host little egret  [6]  *Rocahepevirus ratti*from *Rattus norvegicus* the binomial name of the host, Norway rat [4]  *Rocahepevirus eothenomi*  from Eothenomys melanogaster, the binomial name of the host[12],  [10]  *Chirohepevirus eptesici* from *Eptesicus serotinus* the binomial of the host  [3]  *Chirohepevirus rhinolophi*from *Rhinolophus ferrumequinum* the binomial of the host [11]  *Chirohepevirus desmodi* from *Desmodus rotundus* the binomial of the host  [2]  *Piscihepevirus heenan*from  Heenan Lake, the place of isolation | |

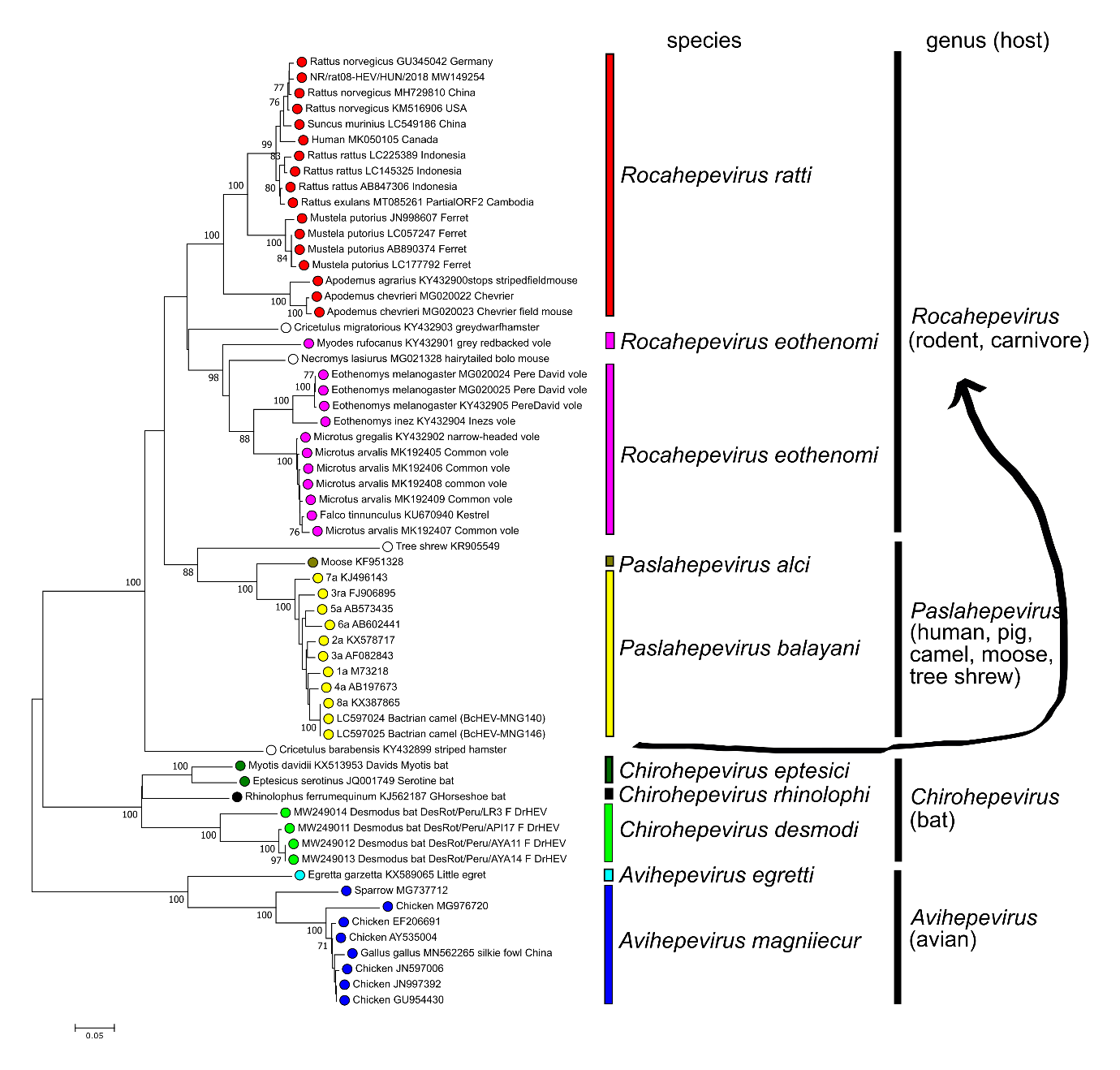
**Supporting evidence**



**Figure 1** Phylogenetic analysis of ORF1 amino acid positions 1−450 (methyltransferase)



**Figure 2** Phylogenetic analysis of ORF1 amino acid positions 971−1692 (RNA-directed RNA polymerase)



**Figure 3** Phylogenetic analysis of ORF2 amino acid positions 121−473 (capsid protein excluding region encoded by overlapping ORF3). The anomalous position of the hamster virus KY432899 relative to the other phylogenetic trees is indicated by an arrow.

**References**

1. Balayan MS, Andjaparidze AG, Savinskaya SS, Ketiladze ES, Braginsky DM, Savinov AP, Poleschuk VF (1983) Evidence for a virus in non-A, non-B hepatitis transmitted via the fecal-oral route. Intervirology 20:23-31 [PMID 6409836]

2. Bergner LM, Mollentze N, Orton RJ, Tello C, Broos A, Biek R, Streicker DG (2021) Characterizing and evaluating the zoonotic potential of novel viruses discovered in vampire bats. Viruses 13:252 [PMID 33562073]

3. Drexler JF, Seelen A, Corman VM, Fumie Tateno A, Cottontail V, Melim Zerbinati R, Gloza-Rausch F, Klose SM, Adu-Sarkodie Y, Oppong SK, Kalko EK, Osterman A, Rasche A, Adam A, Muller MA, Ulrich RG, Leroy EM, Lukashev AN, Drosten C (2012) Bats worldwide carry hepatitis E virus-related viruses that form a putative novel genus within the family *Hepeviridae* J Virol 86:9134-9147 [PMID 22696648]

4. Johne R, Heckel G, Plenge-Bonig A, Kindler E, Maresch C, Reetz J, Schielke A, Ulrich RG (2010) Novel hepatitis E virus genotype in Norway rats, Germany. Emerg Infect Dis 16:1452-1455 [PMID 20735931]

5. Lin J, Norder H, Uhlhorn H, Belák S, Widén F (2014) Novel hepatitis E like virus found in Swedish moose. J Gen Virol 95:557-570 [PMID 24296469]

6. Reuter G, Boros Á, Mátics R, Kapusinszky B, Delwart E, Pankovics P (2016) A novel avian-like hepatitis E virus in wild aquatic bird, little egret (*Egretta garzetta*), in Hungary. Infect Genet Evol 46:74-77 [PMID 27876615]

7. Ryll R, Heckel G, Corman VM, Drexler JF, Ulrich RG (2019) Genomic and spatial variability of a European common vole hepevirus. Arch Virol 164:2671-2682 [PMID 31399875]

8. Smith DB, Simmonds P, Jameel S, Emerson SU, Harrison TJ, Meng XJ, Okamoto H, Van der Poel WH, Purdy MA (2014) Consensus proposals for classification of the family *Hepeviridae*. J Gen Virol 95:2223-2232 [PMID 24989172]

9. Wang B, Yang XL, Li W, Zhu Y, Ge XY, Zhang LB, Zhang YZ, Bock CT, Shi ZL (2017) Detection and genome characterization of four novel bat hepadnaviruses and a hepevirus in China. Virol J 14:40 [PMID 28222808]

10. Wang B, Li W, Zhou JH, Li B, Zhang W, Yang WH, Pan H, Wang LX, Bock CT, Shi ZL, Zhang YZ, Yang XL (2018) Chevrier's field mouse (*Apodemus chevrieri*) and Père David's vole (E*othenomys melanogaster*) in China carry orthohepeviruses that form two putative novel genotypes within the species *Orthohepevirus C*. Virol Sin 33:44-58 [PMID 29500690]

11. Wu Z, Yang L, Ren X, He G, Zhang J, Yang J, Qian Z, Dong J, Sun L, Zhu Y, Du J, Yang F, Zhang S, Jin Q (2016) Deciphering the bat virome catalog to better understand the ecological diversity of bat viruses and the bat origin of emerging infectious diseases. ISME J 10:609-620 [PMID 26262818]

12. Wu Z, Lu L, Du J, Yang L, Ren X, Liu B, Jiang J, Yang J, Dong J, Sun L, Zhu Y, Li Y, Zheng D, Zhang C, Su H, Zheng Y, Zhou H, Zhu G, Li H, Chmura A, Yang F, Daszak P, Wang J, Liu Q, Jin Q (2018) Comparative analysis of rodent and small mammal viromes to better understand the wildlife origin of emerging infectious diseases. Microbiome 6:doi: 10.1186/s40168-40018-40554-40169 [PMID 30285857]

13. Yang C, Wang L, Shen H, Zheng Y, Gauger PC, Chen Q, Zhang J, Yoon KJ, Harmon KM, Main RG, Li G (2018) Detection and genomic characterization of new avian-like hepatitis E virus in a sparrow in the United States. Arch Virol 163:2861-2864 [PMID 29971485]