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.

The Word module explains and justifies your proposal. The Excel module is a critical document that will be used to implement the proposed taxonomic changes once they are approved and ratified. If proposals presented in the Word module are not presented accurately in the Excel module, the taxonomic changes cannot proceed.

For guidance, see the notes written in blue, below, and the Help Notes in file Taxonomic\_Proposals\_Help\_2019.

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

|  |  |  |  |
| --- | --- | --- | --- |
| **Code assigned:** | ***2019.004S*** | |  |
| **Short title:** Create two new genera (*Crahelivirus* and *Gruhelivirus*), each with 1 species (*Crahelivirus A* and *Gruhelivirus A*) | | | |
|  | | | |
| **Author(s) and email address(es):** | | | |
| List authors in a single line *Archives of Virology* citation format (e.g. Smith AB, Huang C-L, Santos, F) | | Provide email address for each author in a single line separated by semi-colons | |
| Zell R, Gorbalenya AE, Hovi T, Knowles NJ, Lindberg M, Oberste S, Palmenberg AC, Reuter G, Simmonds P, Skern T, Tapparel C, Wolthers K, Woo P | | roland.zell@med.uni-jena.de; a.e.gorbalenya@lumc.nl; tapani.hovi@thl.fi; nick.knowles@pirbright.ac.uk; michael.lindberg@lnu.se; soberste@cdc.gov; acpalmen@wisc.edu; reuter.gabor@gmail.com; peter.simmonds@ndm.ox.ac.uk; timothy.skern@meduniwien.ac.at; caroline.tapparel@unige.ch; k.c.wolthers@amc.uva.nl; pcywoo@hkucc.hku.hk | |
| **Author(s) institutional address(es) (optional):**   |  | | --- | | Provide institutional addresses, each on a single line followed by author(s) initials (e.g. University of Woolloomooloo [SAB, HCL]) | | Jena University Hospital [RZ]  Leiden University Medical Center [AEG]  National Institute for Health and Welfare [TH]  The Pirbright Institute [NJK]  Linnaeus University Kalmar [ML]  Centers for Disease Control and Prevention [SO]  University of Wisconsin [ACP]  University of Pécs [GR]  University of Oxford [PS]  Medical University of Vienna [TS]  University of Geneve [CT]  Universiteit van Amsterdam [KW]  University of Hong Kong [PW] | | | | |
| **Corresponding author** | | | |
| **Roland Zell** (roland.zell@med.uni-jena.de) | | | |
| **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) | | ***Picornaviridae* Study Group** | |
| **ICTV Study Group comments (if any) and response of the proposer:** | | | |
|  | | | |
|  | | | |
| Date first submitted to ICTV: | | | 21/05/2019 |
| Date of this revision (if different to above): | | |  |

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

**Part 2:** **NON-STANDARD**

Template for any proposal regarding ICTV procedures, rules or policy, not involving the creation of new taxonomy.

| **Text of proposal:** |
| --- |
|  |

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

|  |
| --- |
| **Name of accompanying Excel module: 2019.004S.N.v1.2newgen\_Craheli-Gruhelivirus.xlsx** |

The taxonomic changes you are proposing should be presented on an accompanying Excel module, 2019\_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, please provide a tree where branch length is **proportional to genetic** distance, generated using an appropriate algorithm (Neighbour-Joining, Maximum Likelihood, or Bayesian) and provide evidence of the reliability of the branching (e.g., by bootstrapping).   Please refer to the Help Notes file (Taxonomic\_Proposals\_Help\_2019) for more information. |

Create one two genera(***Crahelivirus*** and ***Gruhelivirus***), eachwith one species (***Crahelivirus A*** and ***Gruhelivirus A***)

Six novel picornaviruses have been detected in faecal samples of red-crowned cranes (*Grus japonensis*) collected in China, 2014, two of which--crahelivirus A1 and gruhelivirus A1--show similarity to hepatoviruses (Wang et al., 2018). 66.9% divergence of the polyproteins of the two hepato-like viruses suggest two genera rather than two species of one genus.

**A.** **Genus** ***Crahelivirus***

**Relation to other picornaviruses:**

- Crahelivirus has a typical picornavirus genome layout:

5'-UTR[1A-1B-1C-1D/2A-2B-2Chel/3A-3BVPg-3Cpro-3Dpol]3'UTR

(compare Figure 1 in Supporting Material)

- Crahelivirus possesses typical hallmarks of picornaviruses:

**Capsid proteins:** 1B, 1C, 1D have **rhv** domains with drug-binding site,

**2Chel:** **G**xx**G**x**GKS** motif of helicases,

**3BVPg:** **Y-3** residue

**3Cpro:** **C**x**CG**x15**G**x**H** motif,

**3Dpol:** **KDE**, **QSG**, **YGDD**, **FLKR** motifs.

- **Phylogenetic analyses** indicate a distinct branch in the P1 and 3CD trees that clusters with sequences of picornavirus supergroup 5 (*Hepatovirus/Tremovirus*) and some unclassified viruses (compare Figs. 2 & 3 of supporting material).

**Distinguishing features of craheliviruses compared to gruhelivirus and viruses of picornavirus supergroup 5:**

- **Sequence divergence** (uncorrected p-distances) of orthologous proteins is high in pairwise comparisons: The amino acid divergence is greater 60% for P1 and greater 55% for the proteins 2Chel, 3Cpro and 3Dpol of crahelivirus compared to protein sequences of any acknowleged or proposed species of the picornavirus supergroup 5 (compare Table 1). Divergence to sequences of other picornavirus supergroups is even greater.

**Table 1: Amino acid divergence\***

**crahelivirus A1 vs. member of ... P1 2Chel 3Cpro 3Dpol**

*Fipivirus*† *Fipivirus A*† 0.730 0.714 0.768 0.755

*Fipivirus B*† 0.749 0.711 0.820 0.778

*Fipivirus C*† 0.761 0.705 0.776 0.755

*Fipivirus D*† 0.749 0.693 0.824 0.726

*Fipivirus E*† 0.712 0.711 0.864 0.750

*Gruhelivirus*† *Gruhelivirus B*† 0.652 0.636 0.590 0.655

*Hepatovirus Hepatovirus A* 0.604 0.554 0.551 0.640

*Hepatovirus B*  0.601 0.560 0.525 0.617

*Hepatovirus C* 0.612 0.589 0.502 0.643

*Hepatovirus D* 0.606 0.584 0.544 0.622

*Hepatovirus E* 0.601 0.518 0.556 0.629

*Hepatovirus F* 0.613 0.602 0.548 0.640

*Hepatovirus G* 0.600 0.551 0.535 0.632

*Hepatovirus H* 0.602 0.572 0.507 0.611

*Hepatovirus I* 0.606 0.561 0.553 0.654

*Rohelivirus*† *Rohelivirus A*† 0.738 0.648 0.786 0.703

*Tremovirus* *Tremovirus A* 0.645 0.627 0.575 0.675

*Tremovirus B*† 0.645 0.618 0.620 0.651

*unassigned*  Guangdong fish caecilians picornavirus 0.657 0.651 0.678 0.689

\* number of amino acid differences per site

† proposed taxa

- Based on sequence similarity to other viruses of supergroup 5, it is assumed that crahelivirus A1 has an **AUG start codon** at nt positions 632. The deduced 1A protein (VP4) has a length of 19 amino acids. The adjacent 5'-UTR sequence is very similar to that of gruhelivirus A1, but only crahelivirus A1 has an alternative in-frame start codon at nt 572 which would yield a 1A protein of 39 aa. The significance of the alternative start codon is unclear.

- An unusual aa sequences at the **3A-3B** processing site (G↓G) challenges the assumption of an **Y-3**-residue of the 3B peptide; alternative cleavages at adjacent S↓G or E↓S sequences would result in **3B** peptides with an **Y-4** and **Y-5** residue, respectively.

Presumed cleavage site Alternative cleavage site

Crahelivirus A1: AKQ**ESG**↓**G**AY1487 AKQ**ES**↓**GG**AY1487

AKQ**E**↓**SGG**AY1487

**Type species of genus:**

***Crahelivirus A***, crahelivirus A1 (crane picornavirus 1) strain yc-1, GenBank acc. no. KY312540

**Species demarcation criteria:**

not applicable

**Origin of name:**

**Crahelivirus**: derived from **cra**ne (host) and **he**pato-**li**ke **virus**

| **References:** |
| --- |
| Wang Y, Yang S, Liu D, Zhou C, Li W, Lin Y, Wang X, Shen Q, Wang H, Li C, Zong M, Ding Y, Song Q, Deng X, Qi D, Zhang W, Delwart E. The fecal virome of red-crowned cranes. Arch Virol. 2018 Sep 17. doi: 10.1007/s00705-018-4037-x. |

**B.** **Genus** ***Gruhelivirus***

**Relation to other picornaviruses:**

- Gruhelivirus has a typical picornavirus genome layout:

5'-UTR[1A-1B-1C-1D/2A-2B-2Chel/3A-3BVPg-3Cpro-3Dpol]?

The gruhelivirus A1 genome is incomplete: >98% of the polyprotein-encoding sequence plus the 5'UTR is available, but the 3'-end is missing (i.e., 75-90 nt of the 3Dpol gene region [corresponding to 25-30 aa at the C-terminus of the polyprotein] plus the 3'-UTR)

(compare Figure 1 in Supporting Material)

- Gruheliviruses possess typical hallmarks of picornaviruses:

**Capsid proteins:** 1B, 1C, 1D have **rhv** domains with drug-binding site,

**2Chel:** **G**xx**G**x**GKT** motif of helicases,

**3BVPg:** **Y-3** residue

**3Cpro:** **C**x**CG**x15**G**x**H** motif,

**3Dpol:** **KDE**, **PSG**, **YGDD**, **FLKR** motifs.

- Phylogenetic analysis indicates a distinct branch in the P1 and 3CD trees that clusters with sequences of picornavirus supergroup 5 (*Hepatovirus/Tremovirus*) and some unclassified viruses (compare Figs. 2 & 3 of supporting material).

**Distinguishing features of gruheliviruses compared to crahelivirus and other viruses of picornavirus supergroup 5:**

- **Sequence divergence** (uncorrected p-distances) of orthologous proteins is high in pairwise comparisons: The amino acid divergence is greater 55% for P1 and greater 50% for the proteins 2Chel, 3Cpro and 3Dpol of gruhelivirus compared to protein sequences of any acknowleged or proposed species of the picornavirus supergroup 5 (compare Table 1). Divergence to sequences of other picornavirus supergroups is even greater.

**Table 1: Amino acid divergence\***

**gruhelivirus A1 vs. member of ... P1 2Chel 3Cpro 3Dpol**

*Crahelivirus*† *Crahelivirus B*† 0.652 0.636 0.590 0.655

*Fipivirus*† *Fipivirus A*† 0.733 0.739 0.803 0.716

*Fipivirus B*† 0.758 0.744 0.802 0.740

*Fipivirus C*† 0.760 0.729 0.756 0.712

*Fipivirus D*† 0.734 0.711 0.775 0.701

*Fipivirus E*† 0.730 0.735 0.807 0.745

*Hepatovirus Hepatovirus A* 0.580 0.649 0.547 0.646

*Hepatovirus B*  0.572 0.594 0.538 0.614

*Hepatovirus C* 0.577 0.635 0.514 0.639

*Hepatovirus D* 0.567 0.616 0.542 0.658

*Hepatovirus E* 0.583 0.626 0.561 0.653

*Hepatovirus F* 0.581 0.631 0.542 0.662

*Hepatovirus G* 0.585 0.606 0.533 0.664

*Hepatovirus H* 0.584 0.631 0.533 0.660

*Hepatovirus I* 0.599 0.629 0.505 0.659

*Rohelivirus*† *Rohelivirus A*† 0.740 0.649 0.790 0.717

*Tremovirus* *Tremovirus A* 0.593 0.639 0.598 0.655

*Tremovirus B*† 0.613 0.588 0.693 0.662

*unassigned*  Guangdong fish caecilians picornavirus 0.646 0.622 0.665 0.670

\* number of amino acid differences per site

† proposed taxa

**Type species of genus:**

***Gruhelivirus A***, gruhelivirus A1 (crane picornavirus 2) strain yc-2, GenBank acc. no. KY312541

**Species demarcation criteria:**

not applicable

**Origin of name:**

**Gruhelivirus**: derived from ***Gru****s japonensis* (host) and **he**pato-**li**ke **virus**

| **References:** |
| --- |
| Wang Y, Yang S, Liu D, Zhou C, Li W, Lin Y, Wang X, Shen Q, Wang H, Li C, Zong M, Ding Y, Song Q, Deng X, Qi D, Zhang W, Delwart E. The fecal virome of red-crowned cranes. Arch Virol. 2018 Sep 17. doi: 10.1007/s00705-018-4037-x. |

**Supporting material:**



**Legend to Figure 1:** Genomes of craheli- and gruheliviruses compared to the genome of hepatitis A virus (schematic depiction). The open reading frame is indicated by a box. Positions of putative 3Cpro cleavage sites are indicated by a ▼. The VP0 processing site is indicated by a hash (#). The names and lengths of the deduced proteins are presented. The 5'-UTRs of craheli- and gruheliviruses may be incomplete.



**Legend to Figure 2:**  Phylogenetic analysis of picornavirus **P1** using Bayesian tree inference (MrBayes 3.2). Thirty-five picornavirus sequences of the *Hepatovirus/Tremovirus* supergroup were retrieved from GenBank; the cardiovirus sequence served as outgroup. [Note: the supergroup does not imply a taxonomic entity but reflects phylogenetic clustering of the respective genera observed in different tree inference methods (NJ, ML, Bayesian MCMC).] Presented are GenBank accession numbers, ***genus*** ***names***, *species names*, type and—if available—common names in round brackets. Designations of isolates are given in square brackets. Yet unassigned viruses are printed in blue. The proposed names are printed in red and indicated by a dot (●). Numbers at nodes indicate posterior probabilities obtained after 2,000,000 generations. The optimal substitution model (GTR+G+I) was determined with MEGA 5. The scale indicates substitutions/site.



**Legend to Figure 3:**  Phylogenetic analysis of picornavirus **3CD** using Bayesian tree inference (MrBayes 3.2). Thirty-seven picornavirus sequences of the *Hepatovirus/Tremovirus* supergroup were retrieved from GenBank; the cardiovirus sequence served as outgroup. [Note: the supergroup does not imply a taxonomic entity but reflects phylogenetic clustering of the respective genera observed in different tree inference methods (NJ, ML, Bayesian MCMC).] Presented are GenBank accession numbers, ***genus*** ***names***, *species names*, type and—if available—common names in round brackets. Designations of isolates are given in square brackets. Yet unassigned viruses are printed in blue. The proposed name is printed in red and indicated by a dot (●). Numbers at nodes indicate posterior probabilities obtained after 2,000,000 generations. The optimal substitution model (GTR+G+I) was determined with MEGA 5. The scale indicates substitutions/site.