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:** | **2019.003S** | |  |
| **Short title:**  Create 3 new species (*Cardiovirus D, Cardiovirus E and Cardiovirus F*) in the genus *Cardiovirus* | | | |
|  | | | |
| **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:** | | | |
| Remove genet fecal theilovirus (proposed *Cardiovirus E*) and marmot cardiovirus (proposed *Cardiovirus F*) since their representative sequences do not contain complete polyprotein-coding regions.  Response: These two proposals have been removed and red-backed vole cardiovirus and grey-backed vole cardiovirus (originally proposed as *Cardiovirus G* and *Cardiovirus H*) have instead been proposed as *Cardiovirus E* and *Cardiovirus F*, respectively. | | | |
|  | | | |
| Date first submitted to ICTV: | | | 21/05/2019 |
| Date of this revision (if different to above): | | | 20/08/2019 |

|  |
| --- |
| **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:** 2019.003S.A.v1.5newsp\_Cardiovirus\_D-F.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 three new species (*Cardiovirus D, Cardiovirus E and Cardiovirus F*) in the genus *Cardiovirus***

**Cardiovirus hosts:**

Cardioviruses have a broad host range. Since the 1930s, encephalomyocarditis viruses (EMCVs) and Theiler's murine encephalomyelitis viruses (TMEVs) have been detected in humans, apes, monkeys, pigs, mice and rats. In the recent years, novel cardioviruses have been identified in humans, voles, genets, and marmots: The Saffold viruses (proposed cardioviruses D1 to D11) are human cardioviruses with global distribution (Jones et al. 2007). They were previously classified within the species *Cardiovirus B*. Two other cardioviruses (cardiovirus E1 and F1) were detected in pharyngeal or anal swabs of captured northern red-backed voles (*Myodes rutilus*) and grey-backed voles (*Myodes rufocanus*) from the Jilin province of China (Wu et al. 2018). Genet fecal theilovirus was detected in a rectal swab of a dead common genet (*Genetta genetta*) in Spain (Bodewes et al. 2014) and marmot cardiovirus was detected in the intestinal contents of captured Himalayan marmots (*Marmota himalayana*) from the Qinghai-Tibetan Plateau, China (Luo et al. 2018), however, neither of the genome sequences of these viruses are currently complete enough for formal classification as new species. None of these new viruses, with the exception of some Saffold viruses, have been isolated.

**Relation to known cardioviruses:**

- The novel viruses have the typical cardiovirus genome layout:

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

- All deduced protein sequences show a significant homology to the EMCV and TMEV proteins.

- Phylogenetic analyses indicate distinct branches and clades that cluster with the cardioviruses (compare **Figures 1 & 2** of supporting material); all members of the genus *Cardiovirus* present as a monophyletic branch (compare **Figures 3 & 4**).

- Cardioviruses except members of *Cardiovirus C* have a long 2A protein with C-terminal NPGP motive. Length of 2A protein: *Cardiovirus A*: 143-153 aa

*Cardiovirus B*: 133 aa

*Cardiovirus C*: 128 aa (no NPGP motif)

proposed *Cardiovirus D*: 133 aa

proposed *Cardiovirus E*: 133 aa

proposed *Cardiovirus F*: 132 aa

genet fecal theilovirus: 131 aa

marmot cardiovirus: 134 aa

**Distinguishing features of *Cardiovirus D*, *Cardiovirus E* and *Cardiovirus F* compared to the other cardioviruses:**

- Length of leader protein:

*Cardiovirus A* (EMCV): 67 aa

*Cardiovirus B* (TMEV): 76-77 aa

*Cardiovirus C*: 96 aa

proposed *Cardiovirus D* (Saffold viruses): 71 aa

proposed *Cardiovirus E* (red-backed vole cardiovirus): 95 aa (insertion of 18 aa at

C-terminus)

proposed *Cardiovirus F* (grey-backed vole cardiovirus): 89 aa (A833UG) or 77 aa (A869UG)

due to 2 alternative start codons

genet fecal theilovirus: 75 aa; an alternative L\* was proposed

marmot cardiovirus: -- (5'-end of genome missing)

- The 2B proteins of the various cardiovirus species show little similarity.

- The 3A and 3B proteins of cardiovirus D to F show close similarity to the respective cardiovirus B proteins.

- By convention, picornavirus types and species are distinguished on the basis of genus-specific amino acid divergences (compare **Table 1**). Available divergence estimates justify the proposal of three new species, named *Cardiovirus D, Cardiovirus E* and *Cardiovirus F* (compare Tables 2-5 of supporting material). Species identification follows a 3-step procedure: (i) According to species demarcation rules, p-distances of **polyprotein** sequences greater 30% indicate a new species; in fact, available cardiovirus polyprotein sequences show less than 25% divergence within species and greater 40% between species (highlighted in green, **Table 2**). (ii) *Within species* comparisons of **P1** sequences of a cardioviruses are expected to yield p-distances <30%, observed are p-distances <25% (highlighted in cyan; Table 4); p-distances <10% are interpreted as *within type* comparisons (highlighted in yellow, Table 4). (iii) *Within species* comparisons of cardiovirus **2C-3CD** sequences yield p-distances <20% which meets the species demarcation rule (<30%). Types of a species are defined by comparison of the most divergent genome region, i.e. the VP1 sequences which may show p-distances up to 15%.

**Table 1: Divergence estimates\* of cardiovirus amino acid sequence (summary)**

Polyprotein VP1 P1 2C-3CD†

(Table 2) (Table 3) (Table 4) (Table 5)

Within type <15% <15% <10% <15%

Between types/within species <25% 20-35% 11-25% <20%

Between species/within genus 35-60% 40-67% 35-50% 20-55%

Between genera >60% 65-85% >60% >60%

\* p-distances

† unsuited for distinction of types

**Exemplar:**

***Cardiovirus D*:** cardiovirus D1 (Saffold virus 1) strain California/81, GenBank acc. no. EF165067

***Cardiovirus E*:** cardiovirus E1 (red-backed vole cardiovirus) strain RtMruf-PicoV/JL2014-1, GenBank acc. no. KY432930

***Cardiovirus F*:** cardiovirus F1 (grey-backed vole cardiovirus) strain RtMrut-PicoV/JL2014-1, GenBank acc. no. KY432928

**Species demarcation criteria:**

Members of a species of the genus *Cardiovirus*:

- are less than 30% divergent in polyprotein aa sequence (compare Table 2),

-are less than 30% divergent in P1 aa sequence (compare Table 4),

-are less than 30% divergent in 2C+3CD aa sequence (compare Table 5),

- share a common genome organization,

- share a natural host range which is very wide in *Cardiovirus A*, but as far as is known, narrow in the other species.

| **References:** |
| --- |
| 1. Jones MS, Lukashov VV, Ganac RD, Schnurr DP. 2007. Discovery of a novel human picornavirus from a pediatric patient presenting with fever of unknown origin. J Clin Microbiol 45: 2144-2150  2. 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 6:178.  3. Bodewes R, Ruiz-Gonzalez A, Schapendonk CME, van den Brand JMA, Osterhaus ADME, Smits SL. 2014. Viral metagenomics analysis of feces of wild small carnivores. Virology J 11:89.  4. Luo XL, Lu S, Jin D, Yang J, Wu SS, Xu J. 2018. *Marmota himalayana* in the Qinghai-Tibetan plateau as a special host for bi-segmented and unsegmented picobirnaviruses. Emerg Microbes Infections 7:20 |

**Supporting material:**



**Figure 1:** Phylogenetic analysis of cardiovirus **P1** nucleotide sequences using Bayesian tree inference (MrBayes 3.2). Forty-one cardiovirus sequences were retrieved from GenBank. Presented are GenBank accession numbers, types and—if available—common names (in round brackets). Designations of isolates are given in square brackets. The proposed name is printed in red and indicated by a dot (●). Recombinant thera viruses are shaded. 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.



**Figure 2:** Phylogenetic analysis of nucleotide sequences encoding cardiovirus **2C-3CD** proteins using Bayesian tree inference (MrBayes 3.2). Thirty-nine cardiovirus sequences were retrieved from GenBank. Presented are GenBank accession numbers, types and—if available—common names (in round brackets). Designations of isolates are given in square brackets. The proposed name is printed in red and indicated by a dot (●). Recombinant thera viruses are shaded. 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 **P1** using Bayesian tree inference (MrBayes 3.2). Seventy-six picornavirus sequences of the *Ailurivirus/Aphthovirus/Bopivirus/Cardiovirus/Cosavirus/Erbovirus/ Hunnivirus/Malagasivirus/Mischivirus/Mosavirus/Senecavirus/Teschovirus/Torchivirus/Tottorivirus* supergroup were retrieved from GenBank; the enterovirus 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. Proposed names are printed in red and indicated by a dot (●). Numbers at nodes indicate posterior probabilities obtained after 1,000,000 generations. The optimal substitution model (GTR+G+I) was determined with MEGA 5. The scale indicates substitutions/site.



**Legend to Figure 4:**  Phylogenetic analysis of picornavirus **3CD** using Bayesian tree inference (MrBayes 3.2). Seventy-two picornavirus sequences of the *Ailurivirus/Aphthovirus/Bopivirus/Cardiovirus/Cosavirus/Erbovirus/ Hunnivirus/Malagasivirus/Mischivirus/Mosavirus/Senecavirus/Teschovirus/Torchivirus/Tottorivirus* supergroup were retrieved from GenBank; the enterovirus 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. 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.

**Table 2. Estimates of Evolutionary Divergence between Polyprotein Sequences of Cardioviruses**

[ 1] M81861, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [R]

[ 2] KP892662, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [MM]

[ 3] AY296731, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [EMCV-30]

[ 4] KM269482, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [ATCC VR-129B]

[ 5] L22089, *Cardiovirus A*, cardiovirus A1 (Mengo virus) [M]

[ 6] EU780148, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [K3]

[ 7] M37588, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [D variant ifp- phenotype]

[ 8] DQ835185, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [1086C]

[ 9] KC310737, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [Sing-M100-02]

[10] JX257003, *Cardiovirus A*, cardiovirus A2 (EMCV-2) [RD 1338 (D28/05)]

[11] M20562, *Cardiovirus B*, cardiovirus B1 (TMEV) [GDVII]

[12] M20301, *Cardiovirus B*, cardiovirus B1 (TMEV) [DA]

[13] M16020, *Cardiovirus B*, cardiovirus B1 (TMEV) [BeAn 8386]

[14] EU718732, *Cardiovirus B*, cardiovirus B1 (TMEV) [TO B15]

[15] EU723238, *Cardiovirus B*, cardiovirus B1 (TMEV) [TO Yale]

[16] KJ191558, *Cardiovirus B*, cardiovirus B1 [Sikhote-Alin P-113/Russia/1970]

[17] MF172923, *Cardiovirus B*, cardiovirus B3 (rodent cardiovirus) [Rattus rattus/China/2014]

[18] AB090161, *Cardiovirus B*, cardiovirus B4 (theravirus) [NGS910]

[19] EU542581, *Cardiovirus B*, cardiovirus B4 (theravirus) [RTV-1]

[20] MF416403, *Cardiovirus B*, cardiovirus B5 [NYC/Manhattan/poolF4]

[21] JQ864242, *Cardiovirus C*, cardiovirus C1 (Boone cardiovirus 1) [BCV-1]

[22] JX683808, *Cardiovirus C*, cardiovirus C2 (Boone cardiovirus 2) [BCV-2]

[23] MF352424, *Cardiovirus C*, cardiovirus C3 [Wencheng-Rn416]

[24] EF165067, *Cardiovirus D*, cardiovirus D1 (Saffold virus 1) [California/81]

[25] JF813004, *Cardiovirus D*, cardiovirus D2 (Saffold virus 2) [Can112051-06]

[26] EU681178, *Cardiovirus D*, cardiovirus D3 (Saffold virus 3) [D/VI2273/2004]

[27] AB747251, *Cardiovirus D*, cardiovirus D4 (Saffold virus 4) [Pak-3164]

[28] FJ463615, *Cardiovirus D*, cardiovirus D5 (Saffold virus 5) [Pak5003]

[29] FJ463617, *Cardiovirus D*, cardiovirus D6 (Saffold virus 6) [Pak6572]

[30] AB747254, *Cardiovirus D*, cardiovirus D7 (Saffold virus 7) [Pak-2106]

[31] AB747255, *Cardiovirus D*, cardiovirus D8 (Saffold virus 8) [Pak-3486]

[32] AB747256, *Cardiovirus D*, cardiovirus D9 (Saffold virus 9) [Pak-2457]

[33] AB747257, *Cardiovirus D*, cardiovirus D10 (Saffold virus 10) [Pak-2325]

[34] AB747258, *Cardiovirus D*, cardiovirus D11 (Saffold virus 11) [Pak-2338]

[35] KF823815, genet fecal theilovirus [S15]

[36] KY855434, marmot cardiovirus [HT7]

[37] KY432928, *Cardiovirus E*, cardiovirus E1 [RtMrut-PicoV/JL2014-1]

[38] KY432930, *Cardiovirus F*, cardiovirus F1 [RtMruf-PicoV/JL2014-1]

[ 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 ]

[ 1]

[ 2] 0.068

[ 3] 0.040 0.063

[ 4] 0.008 0.062 0.035

[ 5] 0.064 0.075 0.060 0.062

[ 6] 0.012 0.066 0.038 0.005 0.066

[ 7] 0.045 0.067 0.045 0.040 0.062 0.044

[ 8] 0.054 0.067 0.055 0.049 0.050 0.054 0.056

[ 9] 0.138 0.140 0.136 0.133 0.134 0.136 0.136 0.131

[10] 0.186 0.191 0.185 0.182 0.175 0.185 0.185 0.179 0.174

[11] 0.452 0.450 0.448 0.449 0.452 0.451 0.451 0.451 0.451 0.459

[12] 0.448 0.449 0.446 0.446 0.448 0.448 0.447 0.446 0.451 0.460 0.054

[13] 0.449 0.447 0.446 0.446 0.448 0.448 0.448 0.446 0.453 0.459 0.043 0.044

[14] 0.450 0.451 0.447 0.448 0.450 0.450 0.450 0.451 0.454 0.464 0.046 0.051 0.031

[15] 0.454 0.454 0.451 0.451 0.454 0.453 0.453 0.453 0.456 0.464 0.046 0.048 0.041 0.039

[16] 0.448 0.449 0.446 0.446 0.448 0.449 0.450 0.448 0.450 0.459 0.054 0.051 0.051 0.061 0.060

[17] 0.464 0.466 0.460 0.462 0.463 0.465 0.460 0.462 0.463 0.465 0.165 0.163 0.166 0.167 0.170 0.157

[18] 0.454 0.453 0.449 0.452 0.453 0.454 0.449 0.449 0.456 0.460 0.217 0.211 0.211 0.216 0.222 0.211 0.203

[19] 0.455 0.453 0.450 0.452 0.453 0.455 0.449 0.450 0.456 0.459 0.216 0.207 0.207 0.217 0.220 0.207 0.203 0.019

[20] 0.457 0.460 0.455 0.455 0.456 0.457 0.454 0.457 0.456 0.462 0.107 0.106 0.102 0.108 0.112 0.104 0.159 0.211 0.208

[21] 0.551 0.554 0.549 0.549 0.552 0.551 0.554 0.549 0.559 0.561 0.534 0.535 0.534 0.538 0.538 0.536 0.536 0.541 0.541 0.530

[22] 0.580 0.584 0.576 0.579 0.580 0.580 0.580 0.578 0.590 0.586 0.557 0.557 0.557 0.560 0.561 0.560 0.559 0.564 0.564 0.550 0.087

[23] 0.548 0.551 0.546 0.546 0.548 0.549 0.550 0.546 0.552 0.555 0.531 0.532 0.532 0.536 0.538 0.534 0.534 0.539 0.539 0.528 0.073 0.069

[24] 0.465 0.467 0.461 0.463 0.464 0.466 0.460 0.462 0.468 0.469 0.282 0.279 0.283 0.287 0.291 0.278 0.279 0.226 0.225 0.279 0.543 0.559 0.538

[25] 0.459 0.464 0.454 0.458 0.459 0.461 0.457 0.456 0.465 0.465 0.289 0.286 0.288 0.295 0.297 0.287 0.285 0.236 0.238 0.290 0.541 0.560 0.537 0.086

[26] 0.469 0.471 0.462 0.467 0.469 0.470 0.464 0.465 0.471 0.470 0.285 0.281 0.284 0.289 0.293 0.281 0.283 0.237 0.236 0.284 0.544 0.567 0.543 0.096 0.105

[27] 0.463 0.465 0.458 0.461 0.462 0.464 0.459 0.460 0.466 0.466 0.287 0.283 0.286 0.292 0.295 0.283 0.284 0.237 0.240 0.284 0.538 0.557 0.538 0.071 0.072 0.096

[28] 0.473 0.475 0.468 0.471 0.473 0.474 0.467 0.470 0.472 0.472 0.287 0.286 0.286 0.294 0.298 0.288 0.287 0.241 0.242 0.291 0.550 0.573 0.549 0.099 0.112 0.107 0.103

[29] 0.469 0.470 0.463 0.467 0.469 0.470 0.465 0.468 0.470 0.472 0.296 0.294 0.297 0.303 0.307 0.294 0.293 0.243 0.244 0.296 0.551 0.573 0.551 0.106 0.118 0.114 0.106 0.068

[30] 0.469 0.472 0.463 0.467 0.469 0.469 0.465 0.466 0.472 0.471 0.287 0.285 0.287 0.292 0.295 0.284 0.281 0.239 0.239 0.285 0.540 0.563 0.541 0.089 0.108 0.086 0.095 0.104 0.107

[31] 0.467 0.469 0.461 0.466 0.467 0.468 0.463 0.463 0.469 0.470 0.288 0.286 0.286 0.292 0.296 0.284 0.287 0.241 0.240 0.289 0.542 0.565 0.542 0.096 0.108 0.072 0.094 0.099 0.106 0.089

[32] 0.461 0.463 0.456 0.459 0.460 0.461 0.456 0.456 0.464 0.468 0.286 0.286 0.284 0.289 0.295 0.283 0.286 0.238 0.239 0.287 0.541 0.562 0.539 0.102 0.111 0.088 0.100 0.110 0.119 0.080 0.092

[33] 0.463 0.464 0.458 0.462 0.463 0.463 0.460 0.459 0.465 0.464 0.290 0.289 0.287 0.294 0.299 0.285 0.290 0.243 0.243 0.287 0.542 0.562 0.541 0.104 0.115 0.089 0.101 0.107 0.116 0.082 0.093 0.060

[34] 0.467 0.470 0.461 0.465 0.466 0.468 0.462 0.462 0.468 0.469 0.284 0.282 0.283 0.291 0.293 0.281 0.283 0.237 0.237 0.285 0.541 0.565 0.538 0.095 0.106 0.075 0.091 0.094 0.103 0.085 0.051 0.089 0.090

[35] 0.485 0.482 0.478 0.482 0.479 0.484 0.474 0.483 0.483 0.493 0.373 0.365 0.371 0.372 0.376 0.365 0.362 0.365 0.364 0.367 0.578 0.580 0.579 0.375 0.376 0.371 0.375 0.380 0.383 0.379 0.372 0.374 0.377 0.372

[36] 0.494 0.490 0.489 0.492 0.488 0.494 0.490 0.488 0.485 0.487 0.404 0.404 0.402 0.400 0.407 0.402 0.403 0.400 0.400 0.405 0.548 0.592 0.550 0.417 0.412 0.413 0.412 0.419 0.423 0.414 0.412 0.414 0.416 0.409 0.457

[37] 0.472 0.471 0.471 0.470 0.471 0.472 0.468 0.470 0.471 0.489 0.423 0.421 0.426 0.425 0.430 0.423 0.424 0.416 0.418 0.427 0.562 0.592 0.560 0.426 0.424 0.430 0.425 0.436 0.433 0.429 0.427 0.428 0.429 0.427 0.450 0.407

[38] 0.449 0.452 0.447 0.446 0.449 0.449 0.446 0.447 0.451 0.455 0.401 0.397 0.396 0.399 0.402 0.395 0.399 0.398 0.398 0.399 0.543 0.579 0.547 0.405 0.406 0.401 0.401 0.416 0.417 0.403 0.406 0.408 0.402 0.404 0.432 0.348 0.382

within type comparison, between types/within species comparison,

between species/within genus comparison, between genera comparison

**Table 3. Estimates of Evolutionary Divergence between VP1 Sequences of Cardioviruses**

[ 1] M81861, Cardiovirus A, cardiovirus A1 (EMCV-1) [R]

[ 2] KP892662, Cardiovirus A, cardiovirus A1 (EMCV-1) [MM]

[ 3] AY296731, Cardiovirus A, cardiovirus A1 (EMCV-1) [EMCV-30]

[ 4] KM269482, Cardiovirus A, cardiovirus A1 (EMCV-1) [ATCC VR-129B]

[ 5] L22089, Cardiovirus A, cardiovirus A1 (EMCV-1) (Mengo virus) [M]

[ 6] JN800423, Cardiovirus A, cardiovirus A1 (EMCV-1) [KNP/19/94]

[ 7] EU780148, Cardiovirus A, cardiovirus A1 (EMCV-1) [K3]

[ 8] M37588, Cardiovirus A, cardiovirus A1 (EMCV-1) [D variant ifp-phenotype]

[ 9] AJ617358, Cardiovirus A, cardiovirus A1 (EMCV-1) [I136/86]

[10] DQ835185, Cardiovirus A, cardiovirus A1 (EMCV-1) [rat/BEL-1086C]

[11] KC310737, Cardiovirus A, cardiovirus A1 (EMCV-1) [Sing-M100-02]

[12] JX257003, Cardiovirus A, cardiovirus A2 (EMCV-2) [RD 1338 (D28/05)]

[13] M20562, Cardiovirus B, cardiovirus B1 (TMEV) [GDVII]

[14] M20301, Cardiovirus B, cardiovirus B1 (TMEV) [DA]

[15] M16020, Cardiovirus B, cardiovirus B1 (TMEV) [BeAn 8386]

[16] EU718732, Cardiovirus B, cardiovirus B1 (TMEV) [TO B15]

[17] EU723238, Cardiovirus B, cardiovirus B1 (TMEV) [TO Yale]

[18] KJ191558, Cardiovirus B, cardiovirus B1 (TMEV) [Sikhote-Alin P-113/Russia/1970]

[19] M94868, Cardiovirus B, cardiovirus B2 (VHEV) [V1/Siberia/55]

[20] MF172923, Cardiovirus B, cardiovirus B3 (rodent cardiovirus 1) [Rattus rattus/China/2014]

[21] AB090161, Cardiovirus B, cardiovirus B4 (theravirus) [NGS910]

[22] EU542581, Cardiovirus B, cardiovirus B4 (theravirus) [RTV-1]

[23] MF416403, Cardiovirus B, cardiovirus B5 [NYC/Manhattan/poolF4]

[24] JQ864242, Cardiovirus C, cardiovirus C1 (Boone cardiovirus 1) [BCV-1]

[25] JX683808, Cardiovirus C, cardiovirus C2 (Boone cardiovirus 2) [BCV-2]

[26] MF352424, Cardiovirus C, cardiovirus C3 [Wencheng-Rn416]

[27] EF165067, Cardiovirus D, cardiovirus D1 (Saffold virus 1) [California/81]

[28] JF813004, Cardiovirus D, cardiovirus D2 (Saffold virus 2) [Can112051-06]

[29] EU681178, Cardiovirus D, cardiovirus D3 (Saffold virus 3) [D/VI2273/2004]

[30] AB747251, Cardiovirus D, cardiovirus D4 (Saffold virus 4) [Pak-3164]

[31] FJ463615, Cardiovirus D, cardiovirus D5 (Saffold virus 5) [Pak5003]

[32] FJ463617, Cardiovirus D, cardiovirus D6 (Saffold virus 6) [Pak6572]

[33] AB747254, Cardiovirus D, cardiovirus D7 (Saffold virus 7) [Pak-2106]

[34] AB747255, Cardiovirus D, cardiovirus D8 (Saffold virus 8) [Pak-3486]

[35] AB747256, Cardiovirus D, cardiovirus D9 (Saffold virus 9) [Pak-2457]

[36] AB747257, Cardiovirus D, cardiovirus D10 (Saffold virus 10) [Pak-2325]

[37] AB747258, Cardiovirus D, cardiovirus D11 (Saffold virus 11) [Pak-2338]

[38] KF823815, genet fecal theilovirus [S15]

[39] KY855434, marmot cardiovirus [HT7]

[40] KY432928, Cardiovirus E, cardiovirus E1 [RtMrut-PicoV/JL2014-1]

[41] KY432930, Cardiovirus F, cardiovirus F1 [RtMruf-PicoV/JL2014-1]

[ 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 ]

[ 1]

[ 2] 0.032

[ 3] 0.022 0.011

[ 4] 0.025 0.014 0.004

[ 5] 0.043 0.043 0.032 0.036

[ 6] 0.043 0.032 0.022 0.025 0.054

[ 7] 0.036 0.029 0.018 0.022 0.047 0.040

[ 8] 0.036 0.032 0.022 0.025 0.043 0.036 0.036

[ 9] 0.033 0.022 0.011 0.015 0.041 0.026 0.030 0.019

[10] 0.025 0.014 0.004 0.007 0.036 0.018 0.022 0.018 0.007

[11] 0.144 0.130 0.134 0.137 0.130 0.137 0.148 0.137 0.130 0.130

[12] 0.339 0.332 0.328 0.328 0.328 0.336 0.339 0.332 0.327 0.332 0.336

[13] 0.519 0.500 0.504 0.504 0.496 0.507 0.511 0.511 0.500 0.507 0.489 0.506

[14] 0.511 0.496 0.496 0.496 0.489 0.500 0.504 0.500 0.492 0.496 0.500 0.513 0.091

[15] 0.519 0.500 0.504 0.504 0.496 0.511 0.511 0.511 0.500 0.507 0.507 0.513 0.072 0.069

[16] 0.515 0.496 0.500 0.500 0.493 0.504 0.507 0.507 0.496 0.504 0.500 0.513 0.072 0.099 0.094

[17] 0.522 0.504 0.507 0.507 0.500 0.507 0.515 0.511 0.500 0.507 0.504 0.513 0.054 0.099 0.083 0.054

[18] 0.504 0.489 0.496 0.496 0.485 0.504 0.507 0.504 0.492 0.500 0.496 0.509 0.101 0.113 0.098 0.120 0.116

[19] 0.511 0.511 0.504 0.504 0.496 0.504 0.515 0.504 0.508 0.507 0.504 0.498 0.283 0.285 0.283 0.297 0.297 0.275

[20] 0.511 0.504 0.500 0.500 0.493 0.496 0.511 0.496 0.496 0.500 0.504 0.498 0.221 0.237 0.225 0.236 0.221 0.225 0.271

[21] 0.522 0.504 0.507 0.507 0.504 0.504 0.519 0.507 0.504 0.504 0.500 0.506 0.272 0.263 0.257 0.268 0.268 0.279 0.304 0.246

[22] 0.522 0.504 0.507 0.507 0.504 0.504 0.519 0.507 0.504 0.504 0.496 0.506 0.261 0.237 0.239 0.268 0.261 0.254 0.297 0.250 0.054

[23] 0.524 0.520 0.517 0.517 0.509 0.517 0.524 0.513 0.513 0.517 0.509 0.504 0.264 0.245 0.250 0.264 0.246 0.264 0.277 0.238 0.275 0.268

[24] 0.643 0.639 0.635 0.635 0.635 0.631 0.643 0.631 0.624 0.635 0.651 0.646 0.593 0.589 0.593 0.601 0.593 0.605 0.592 0.588 0.617 0.613 0.607

[25] 0.633 0.629 0.624 0.624 0.629 0.620 0.633 0.624 0.617 0.624 0.633 0.615 0.563 0.563 0.563 0.567 0.571 0.576 0.562 0.550 0.571 0.563 0.578 0.335

[26] 0.641 0.637 0.633 0.633 0.633 0.629 0.641 0.633 0.627 0.633 0.629 0.629 0.592 0.588 0.596 0.604 0.608 0.612 0.579 0.576 0.604 0.596 0.606 0.339 0.236

[27] 0.529 0.529 0.522 0.522 0.511 0.518 0.537 0.518 0.519 0.518 0.533 0.520 0.426 0.415 0.434 0.441 0.430 0.426 0.401 0.423 0.415 0.401 0.426 0.624 0.575 0.615

[28] 0.511 0.515 0.504 0.504 0.496 0.507 0.519 0.511 0.500 0.504 0.530 0.513 0.424 0.398 0.421 0.435 0.424 0.421 0.432 0.424 0.435 0.432 0.424 0.615 0.578 0.593 0.232

[29] 0.539 0.535 0.528 0.528 0.524 0.532 0.543 0.528 0.529 0.528 0.539 0.508 0.433 0.418 0.433 0.441 0.437 0.437 0.422 0.437 0.441 0.441 0.441 0.607 0.582 0.593 0.321 0.278

[30] 0.519 0.522 0.515 0.515 0.500 0.511 0.530 0.515 0.519 0.515 0.530 0.506 0.458 0.431 0.454 0.465 0.454 0.454 0.454 0.435 0.446 0.446 0.432 0.607 0.576 0.608 0.173 0.173 0.300

[31] 0.537 0.533 0.530 0.530 0.526 0.530 0.541 0.522 0.527 0.526 0.530 0.506 0.421 0.398 0.402 0.435 0.424 0.432 0.432 0.413 0.439 0.439 0.402 0.619 0.582 0.618 0.316 0.357 0.311 0.336

[32] 0.526 0.519 0.515 0.515 0.519 0.522 0.530 0.522 0.527 0.519 0.537 0.521 0.454 0.435 0.443 0.465 0.461 0.446 0.432 0.446 0.450 0.446 0.443 0.619 0.599 0.630 0.338 0.364 0.333 0.343 0.205

[33] 0.524 0.520 0.513 0.517 0.517 0.517 0.524 0.513 0.510 0.513 0.528 0.515 0.412 0.407 0.415 0.430 0.419 0.426 0.397 0.408 0.445 0.438 0.430 0.578 0.569 0.602 0.304 0.309 0.280 0.305 0.298 0.324

[34] 0.528 0.524 0.520 0.520 0.509 0.520 0.535 0.517 0.513 0.517 0.520 0.477 0.444 0.440 0.444 0.456 0.452 0.444 0.437 0.452 0.478 0.467 0.441 0.619 0.591 0.610 0.332 0.333 0.240 0.322 0.300 0.319 0.317

[35] 0.500 0.493 0.489 0.493 0.481 0.493 0.500 0.485 0.492 0.485 0.504 0.513 0.428 0.424 0.424 0.432 0.432 0.424 0.443 0.428 0.454 0.454 0.424 0.601 0.580 0.604 0.353 0.336 0.307 0.343 0.347 0.376 0.268 0.330

[36] 0.515 0.515 0.507 0.511 0.500 0.511 0.515 0.511 0.515 0.507 0.515 0.509 0.450 0.428 0.432 0.458 0.454 0.432 0.424 0.439 0.472 0.465 0.421 0.597 0.563 0.600 0.349 0.354 0.296 0.347 0.328 0.373 0.268 0.322 0.188

[37] 0.539 0.535 0.532 0.532 0.520 0.532 0.546 0.528 0.529 0.528 0.517 0.504 0.422 0.410 0.419 0.441 0.430 0.422 0.426 0.426 0.441 0.437 0.415 0.602 0.565 0.581 0.343 0.311 0.207 0.315 0.296 0.330 0.310 0.162 0.322 0.319

[38] 0.531 0.524 0.516 0.516 0.505 0.520 0.524 0.513 0.513 0.513 0.509 0.530 0.487 0.484 0.495 0.502 0.495 0.491 0.505 0.500 0.502 0.491 0.491 0.593 0.567 0.591 0.504 0.480 0.478 0.478 0.480 0.513 0.489 0.459 0.476 0.487 0.448

[39] 0.602 0.595 0.588 0.588 0.577 0.584 0.595 0.588 0.583 0.584 0.580 0.576 0.522 0.515 0.518 0.522 0.522 0.522 0.511 0.520 0.529 0.526 0.529 0.633 0.626 0.621 0.540 0.554 0.533 0.557 0.561 0.572 0.548 0.533 0.550 0.565 0.544 0.566

[40] 0.618 0.604 0.607 0.607 0.596 0.607 0.618 0.607 0.607 0.607 0.585 0.599 0.601 0.601 0.615 0.612 0.612 0.604 0.620 0.612 0.597 0.612 0.635 0.656 0.655 0.663 0.615 0.607 0.624 0.599 0.636 0.632 0.612 0.624 0.610 0.632 0.624 0.629 0.611

[41] 0.535 0.524 0.520 0.520 0.524 0.524 0.531 0.520 0.521 0.520 0.538 0.518 0.463 0.463 0.463 0.482 0.463 0.467 0.509 0.482 0.511 0.496 0.498 0.610 0.600 0.618 0.536 0.498 0.485 0.522 0.517 0.528 0.515 0.507 0.524 0.517 0.511 0.549 0.470 0.576

within type comparison, between types/within species comparison,

between species/within genus comparison, between genera comparison

**Table 4. Estimates of Evolutionary Divergence between P1 Sequences of Cardioviruses**

[ 1] M81861, Cardiovirus A, cardiovirus A1 (EMCV-1) [R]

[ 2] KP892662, Cardiovirus A, cardiovirus A1 (EMCV-1) [MM]

[ 3] AY296731, Cardiovirus A, cardiovirus A1 (EMCV-1) [EMCV-30]

[ 4] KM269482, Cardiovirus A, cardiovirus A1 (EMCV-1) [ATCC VR-129B]

[ 5] L22089, Cardiovirus A, cardiovirus A1 (EMCV-1) (Mengo virus) [M]

[ 6] JN800423, Cardiovirus A, cardiovirus A1 (EMCV-1) [KNP/19/94]

[ 7] EU780148, Cardiovirus A, cardiovirus A1 (EMCV-1) [K3]

[ 8] M37588, Cardiovirus A, cardiovirus A1 (EMCV-1) [D variant ifp-phenotype]

[ 9] AJ617358, Cardiovirus A, cardiovirus A1 (EMCV-1) [I136/86]

[10] DQ835185, Cardiovirus A, cardiovirus A1 (EMCV-1) [rat/BEL-1086C]

[11] KC310737, Cardiovirus A, cardiovirus A1 (EMCV-1) [Sing-M100-02]

[12] JX257003, Cardiovirus A, cardiovirus A2 (EMCV-2) [RD 1338 (D28/05)]

[13] M20562, Cardiovirus B, cardiovirus B1 (TMEV) [GDVII]

[14] M20301, Cardiovirus B, cardiovirus B1 (TMEV) [DA]

[15] M16020, Cardiovirus B, cardiovirus B1 (TMEV) [BeAn 8386]

[16] EU718732, Cardiovirus B, cardiovirus B1 (TMEV) [TO B15]

[17] EU723238, Cardiovirus B, cardiovirus B1 (TMEV) [TO Yale]

[18] KJ191558, Cardiovirus B, cardiovirus B1 (TMEV) [Sikhote-Alin P-113/Russia/1970]

[19] M94868, Cardiovirus B, cardiovirus B2 (VHEV) [V1/Siberia/55]

[20] MF172923, Cardiovirus B, cardiovirus B3 (rodent cardiovirus 1) [Rattus rattus/China/2014]

[21] AB090161, Cardiovirus B, cardiovirus B4 (theravirus) [NGS910]

[22] EU542581, Cardiovirus B, cardiovirus B4 (theravirus) [RTV-1]

[23] MF416403, Cardiovirus B, cardiovirus B5 [NYC/Manhattan/poolF4]

[24] JQ864242, Cardiovirus C, cardiovirus C1 (Boone cardiovirus 1) [BCV-1]

[25] JX683808, Cardiovirus C, cardiovirus C2 (Boone cardiovirus 2) [BCV-2]

[26] MF352424, Cardiovirus C, cardiovirus C3 [Wencheng-Rn416]

[27] EF165067, Cardiovirus D, cardiovirus D1 (Saffold virus 1) [California/81]

[28] JF813004, Cardiovirus D, cardiovirus D2 (Saffold virus 2) [Can112051-06]

[29] EU681178, Cardiovirus D, cardiovirus D3 (Saffold virus 3) [D/VI2273/2004]

[30] AB747251, Cardiovirus D, cardiovirus D4 (Saffold virus 4) [Pak-3164]

[31] FJ463615, Cardiovirus D, cardiovirus D5 (Saffold virus 5) [Pak5003]

[32] FJ463617, Cardiovirus D, cardiovirus D6 (Saffold virus 6) [Pak6572]

[33] AB747254, Cardiovirus D, cardiovirus D7 (Saffold virus 7) [Pak-2106]

[34] AB747255, Cardiovirus D, cardiovirus D8 (Saffold virus 8) [Pak-3486]

[35] AB747256, Cardiovirus D, cardiovirus D9 (Saffold virus 9) [Pak-2457]

[36] AB747257, Cardiovirus D, cardiovirus D10 (Saffold virus 10) [Pak-2325]

[37] AB747258, Cardiovirus D, cardiovirus D11 (Saffold virus 11) [Pak-2338]

[38] KF823815, genet fecal theilovirus [S15]

[39] KY855434, marmot cardiovirus [HT7]

[40] KY432928, Cardiovirus E, cardiovirus E1 [RtMrut-PicoV/JL2014-1]

[41] KY432930, Cardiovirus F, cardiovirus F1 [RtMruf-PicoV/JL2014-1]

[ 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 ]

[ 1]

[ 2] 0.023

[ 3] 0.018 0.022

[ 4] 0.013 0.014 0.012

[ 5] 0.030 0.035 0.026 0.028

[ 6] 0.030 0.030 0.026 0.024 0.030

[ 7] 0.019 0.020 0.019 0.010 0.034 0.031

[ 8] 0.026 0.028 0.018 0.020 0.030 0.030 0.026

[ 9] 0.023 0.022 0.017 0.012 0.027 0.022 0.019 0.016

[10] 0.018 0.017 0.012 0.010 0.023 0.017 0.017 0.013 0.007

[11] 0.094 0.089 0.091 0.088 0.092 0.092 0.094 0.091 0.085 0.083

[12] 0.242 0.239 0.237 0.236 0.233 0.236 0.241 0.238 0.231 0.236 0.231

[13] 0.385 0.380 0.377 0.377 0.375 0.382 0.382 0.381 0.375 0.379 0.373 0.389

[14] 0.380 0.376 0.375 0.372 0.367 0.376 0.377 0.373 0.369 0.371 0.373 0.391 0.076

[15] 0.382 0.377 0.377 0.375 0.373 0.381 0.380 0.379 0.373 0.376 0.376 0.390 0.051 0.058

[16] 0.386 0.381 0.379 0.379 0.376 0.383 0.383 0.382 0.376 0.380 0.379 0.396 0.051 0.068 0.043

[17] 0.392 0.387 0.385 0.385 0.382 0.388 0.390 0.387 0.381 0.385 0.383 0.399 0.052 0.065 0.046 0.033

[18] 0.376 0.373 0.374 0.371 0.367 0.377 0.377 0.375 0.369 0.373 0.371 0.389 0.070 0.062 0.058 0.070 0.073

[19] 0.393 0.392 0.390 0.387 0.382 0.387 0.391 0.388 0.386 0.387 0.383 0.386 0.213 0.210 0.206 0.217 0.216 0.203

[20] 0.392 0.391 0.386 0.386 0.383 0.389 0.392 0.386 0.384 0.386 0.388 0.392 0.174 0.171 0.169 0.178 0.175 0.163 0.188

[21] 0.391 0.385 0.385 0.383 0.380 0.385 0.388 0.385 0.380 0.381 0.382 0.391 0.201 0.192 0.187 0.196 0.201 0.191 0.206 0.159

[22] 0.392 0.386 0.386 0.385 0.381 0.386 0.390 0.386 0.381 0.382 0.382 0.390 0.199 0.182 0.183 0.199 0.199 0.184 0.205 0.160 0.029

[23] 0.392 0.393 0.388 0.387 0.382 0.389 0.392 0.387 0.383 0.385 0.382 0.388 0.195 0.184 0.186 0.196 0.191 0.187 0.195 0.161 0.184 0.184

[24] 0.499 0.499 0.497 0.494 0.493 0.492 0.499 0.494 0.487 0.492 0.503 0.516 0.470 0.469 0.474 0.477 0.477 0.475 0.474 0.464 0.469 0.470 0.463

[25] 0.488 0.490 0.486 0.483 0.483 0.481 0.488 0.483 0.477 0.481 0.487 0.498 0.458 0.461 0.462 0.465 0.470 0.465 0.460 0.449 0.451 0.451 0.449 0.142

[26] 0.497 0.497 0.494 0.492 0.491 0.489 0.497 0.493 0.486 0.489 0.492 0.509 0.463 0.464 0.468 0.471 0.478 0.471 0.469 0.459 0.466 0.466 0.461 0.145 0.104

[27] 0.391 0.391 0.387 0.386 0.380 0.387 0.392 0.387 0.383 0.384 0.391 0.394 0.305 0.299 0.306 0.312 0.313 0.300 0.299 0.297 0.286 0.282 0.296 0.467 0.455 0.462

[28] 0.379 0.383 0.375 0.375 0.369 0.375 0.382 0.380 0.372 0.374 0.389 0.384 0.321 0.313 0.314 0.325 0.325 0.317 0.328 0.313 0.307 0.311 0.323 0.468 0.452 0.458 0.172

[29] 0.400 0.399 0.393 0.394 0.390 0.395 0.400 0.395 0.390 0.392 0.400 0.396 0.318 0.309 0.313 0.319 0.321 0.308 0.313 0.313 0.311 0.311 0.315 0.475 0.469 0.475 0.214 0.219

[30] 0.388 0.390 0.386 0.383 0.377 0.381 0.390 0.386 0.382 0.382 0.391 0.391 0.317 0.312 0.314 0.323 0.325 0.315 0.327 0.315 0.313 0.317 0.313 0.465 0.452 0.463 0.146 0.127 0.208

[31] 0.419 0.416 0.414 0.414 0.407 0.407 0.419 0.410 0.408 0.409 0.410 0.408 0.323 0.320 0.317 0.329 0.333 0.330 0.331 0.327 0.330 0.331 0.331 0.492 0.486 0.496 0.223 0.234 0.236 0.230

[32] 0.403 0.399 0.397 0.397 0.392 0.393 0.403 0.398 0.396 0.394 0.400 0.402 0.331 0.327 0.330 0.340 0.344 0.329 0.331 0.325 0.324 0.324 0.332 0.483 0.481 0.490 0.226 0.238 0.239 0.233 0.130

[33] 0.403 0.405 0.398 0.398 0.394 0.397 0.401 0.399 0.393 0.395 0.406 0.403 0.328 0.324 0.325 0.334 0.333 0.322 0.315 0.316 0.324 0.323 0.319 0.466 0.464 0.473 0.201 0.225 0.182 0.216 0.241 0.236

[34] 0.398 0.398 0.394 0.393 0.388 0.394 0.399 0.394 0.388 0.390 0.398 0.396 0.321 0.319 0.318 0.325 0.327 0.315 0.326 0.324 0.331 0.329 0.324 0.478 0.468 0.476 0.221 0.227 0.144 0.210 0.227 0.233 0.204

[35] 0.387 0.385 0.383 0.381 0.377 0.381 0.385 0.381 0.379 0.378 0.389 0.401 0.322 0.329 0.319 0.327 0.332 0.320 0.330 0.326 0.327 0.331 0.320 0.469 0.466 0.471 0.226 0.233 0.186 0.229 0.252 0.257 0.169 0.208

[36] 0.393 0.391 0.390 0.389 0.386 0.387 0.391 0.391 0.388 0.386 0.391 0.394 0.332 0.333 0.325 0.337 0.342 0.326 0.321 0.335 0.334 0.337 0.321 0.472 0.462 0.474 0.225 0.241 0.189 0.230 0.241 0.253 0.185 0.208 0.119

[37] 0.400 0.400 0.396 0.395 0.388 0.394 0.401 0.394 0.389 0.390 0.394 0.399 0.315 0.310 0.312 0.325 0.325 0.312 0.322 0.319 0.320 0.319 0.315 0.471 0.465 0.468 0.219 0.220 0.150 0.209 0.217 0.227 0.208 0.111 0.200 0.206

[38] 0.399 0.395 0.393 0.393 0.386 0.393 0.397 0.394 0.390 0.389 0.394 0.407 0.348 0.338 0.348 0.352 0.351 0.342 0.360 0.335 0.338 0.337 0.340 0.483 0.471 0.483 0.352 0.345 0.344 0.350 0.361 0.361 0.362 0.345 0.353 0.358 0.346

[39] 0.465 0.460 0.454 0.458 0.449 0.455 0.463 0.455 0.453 0.454 0.449 0.448 0.429 0.432 0.429 0.431 0.431 0.431 0.415 0.428 0.432 0.431 0.447 0.517 0.509 0.519 0.458 0.450 0.454 0.465 0.474 0.475 0.466 0.453 0.455 0.466 0.445 0.453

[40] 0.411 0.405 0.408 0.405 0.402 0.408 0.409 0.407 0.403 0.404 0.402 0.429 0.411 0.413 0.423 0.423 0.424 0.417 0.420 0.419 0.412 0.420 0.427 0.509 0.501 0.512 0.434 0.419 0.448 0.426 0.457 0.445 0.441 0.440 0.446 0.450 0.443 0.428 0.469

[41] 0.387 0.384 0.385 0.380 0.381 0.380 0.386 0.381 0.378 0.378 0.390 0.390 0.356 0.356 0.356 0.366 0.360 0.356 0.366 0.353 0.367 0.362 0.364 0.468 0.458 0.471 0.377 0.376 0.365 0.374 0.405 0.398 0.379 0.382 0.387 0.375 0.382 0.380 0.372 0.384

within type comparison, between types/within species comparison,

between species/within genus comparison, between genera comparison

**Table 5. Estimates of Evolutionary Divergence between 2C-3CD Sequences of Cardioviruses**

[ 1] M81861, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [R]

[ 2] KP892662, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [MM]

[ 3] AY296731, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [EMCV-30]

[ 4] KM269482, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [ATCC VR-129B]

[ 5] L22089, *Cardiovirus A*, cardiovirus A1 (Mengo virus) [M]

[ 6] EU780148, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [K3]

[ 7] M37588, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [D variant ifp- phenotype]

[ 8] DQ835185, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [1086C]

[ 9] KC310737, *Cardiovirus A*, cardiovirus A1 (EMCV-1) [Sing-M100-02]

[10] JX257003, *Cardiovirus A*, cardiovirus A2 (EMCV-2) [RD 1338 (D28/05)]

[11] M20562, *Cardiovirus B*, cardiovirus B1 (TMEV) [GDVII]

[12] M20301, *Cardiovirus B*, cardiovirus B1 (TMEV) [DA]

[13] M16020, *Cardiovirus B*, cardiovirus B1 (TMEV) [BeAn 8386]

[14] EU718732, *Cardiovirus B*, cardiovirus B1 (TMEV) [TO B15]

[15] EU723238, *Cardiovirus B*, cardiovirus B1 (TMEV) [TO Yale]

[16] KJ191558, *Cardiovirus B*, cardiovirus B1 [Sikhote-Alin P-113/Russia/1970]

[17] EU723237, *Cardiovirus B*, cardiovirus B2 (VHEV) [V1/Siberia/55]

[18] MF172923, *Cardiovirus B*, cardiovirus B3 (rodent cardiovirus) [Rattus rattus/China/2014]

[19] AB090161, *Cardiovirus B*, cardiovirus B4 (theravirus) [NGS910]

[20] EU542581, *Cardiovirus B*, cardiovirus B4 (theravirus) [RTV-1]

[21] MF416403, *Cardiovirus B*, cardiovirus B5 [NYC/Manhattan/poolF4]

[22] JQ864242, *Cardiovirus C*, cardiovirus C1 (Boone cardiovirus 1) [BCV-1]

[23] JX683808, *Cardiovirus C*, cardiovirus C2 (Boone cardiovirus 2) [BCV-2]

[24] MF352424, *Cardiovirus C*, cardiovirus C3 [Wencheng-Rn416]

[25] EF165067, *Cardiovirus D*, cardiovirus D1 (Saffold virus 19 [California/81]

[26] JF813004, *Cardiovirus D*, cardiovirus D2 (Saffold virus 2) [Can112051-06]

[27] EU681178, *Cardiovirus D*, cardiovirus D3 (Saffold virus 3) [D/VI2273/2004]

[28] AB747251, *Cardiovirus D*, cardiovirus D4 (Saffold virus 4) [Pak-3164]

[29] FJ463615, *Cardiovirus D*, cardiovirus D5 (Saffold virus 5) [Pak5003]

[30] FJ463617, *Cardiovirus D*, cardiovirus D6 (Saffold virus 6) [Pak6572]

[31] AB747254, *Cardiovirus D*, cardiovirus D7 (Saffold virus 7) [Pak-2106]

[32] AB747255, *Cardiovirus D*, cardiovirus D8 (Saffold virus 8) [Pak-3486]

[33] AB747256, *Cardiovirus D*, cardiovirus D9 (Saffold virus 9) [Pak-2457]

[34] AB747257, *Cardiovirus D*, cardiovirus D10 (Saffold virus 10) [Pak-2325]

[35] AB747258, *Cardiovirus D*, cardiovirus D11 (Saffold virus 11) [Pak-2338]

[36] KF823815, genet fecal theilovirus [S15]

[37] KY855434, marmot cardiovirus [HT7]

[38] KY432928, *Cardiovirus E*, cardiovirus E1 [RtMrut-PicoV/JL2014-1]

[39] KY432930, *Cardiovirus F*, cardiovirus F1 [RtMruf-PicoV/JL2014-1]

[ 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 ]

[ 1]

[ 2] 0.083

[ 3] 0.032 0.076

[ 4] 0.003 0.080 0.029

[ 5] 0.068 0.089 0.065 0.067

[ 6] 0.005 0.081 0.031 0.002 0.069

[ 7] 0.038 0.081 0.043 0.035 0.060 0.037

[ 8] 0.061 0.093 0.069 0.060 0.055 0.062 0.066

[ 9] 0.128 0.140 0.126 0.126 0.131 0.127 0.131 0.132

[10] 0.122 0.138 0.122 0.119 0.111 0.121 0.121 0.113 0.107

[11] 0.410 0.410 0.408 0.410 0.417 0.411 0.411 0.411 0.421 0.426

[12] 0.410 0.413 0.408 0.410 0.418 0.411 0.411 0.409 0.421 0.426 0.023

[13] 0.408 0.408 0.406 0.408 0.415 0.409 0.410 0.407 0.423 0.425 0.028 0.030

[14] 0.409 0.412 0.405 0.409 0.414 0.410 0.409 0.411 0.423 0.427 0.029 0.029 0.020

[15] 0.410 0.412 0.409 0.410 0.419 0.411 0.413 0.411 0.422 0.427 0.025 0.023 0.036 0.035

[16] 0.413 0.415 0.409 0.413 0.419 0.414 0.415 0.412 0.423 0.427 0.032 0.039 0.042 0.046 0.040

[17] 0.411 0.417 0.407 0.411 0.417 0.412 0.412 0.412 0.425 0.429 0.037 0.043 0.038 0.034 0.046 0.036

[18] 0.426 0.431 0.422 0.426 0.432 0.427 0.424 0.420 0.430 0.437 0.118 0.120 0.125 0.121 0.127 0.119 0.123

[19] 0.402 0.405 0.400 0.402 0.410 0.403 0.399 0.399 0.413 0.418 0.188 0.185 0.186 0.189 0.193 0.189 0.188 0.185

[20] 0.402 0.405 0.400 0.402 0.410 0.403 0.399 0.399 0.413 0.419 0.188 0.186 0.183 0.188 0.193 0.188 0.186 0.188 0.009

[21] 0.415 0.420 0.411 0.415 0.421 0.416 0.416 0.416 0.423 0.430 0.049 0.056 0.052 0.051 0.061 0.051 0.052 0.124 0.189 0.187

[22] 0.470 0.477 0.470 0.470 0.475 0.471 0.481 0.471 0.481 0.483 0.475 0.479 0.473 0.477 0.476 0.472 0.476 0.480 0.490 0.489 0.475

[23] 0.530 0.540 0.526 0.530 0.531 0.530 0.536 0.530 0.550 0.542 0.531 0.532 0.529 0.534 0.527 0.528 0.532 0.540 0.543 0.543 0.529 0.025

[24] 0.470 0.476 0.468 0.470 0.473 0.471 0.478 0.469 0.479 0.480 0.478 0.481 0.477 0.483 0.480 0.476 0.481 0.484 0.492 0.493 0.478 0.027 0.027

[25] 0.424 0.426 0.416 0.424 0.430 0.425 0.415 0.420 0.426 0.434 0.229 0.225 0.227 0.229 0.233 0.228 0.231 0.223 0.152 0.155 0.232 0.493 0.536 0.494

[26] 0.417 0.422 0.407 0.417 0.422 0.418 0.412 0.411 0.420 0.430 0.228 0.225 0.227 0.229 0.234 0.227 0.227 0.220 0.154 0.157 0.231 0.489 0.535 0.491 0.028

[27] 0.424 0.425 0.412 0.424 0.429 0.425 0.416 0.417 0.425 0.431 0.226 0.220 0.222 0.225 0.229 0.225 0.224 0.220 0.154 0.157 0.226 0.487 0.533 0.489 0.023 0.029

[28] 0.420 0.421 0.409 0.420 0.426 0.421 0.414 0.415 0.422 0.427 0.226 0.221 0.223 0.226 0.230 0.224 0.225 0.217 0.151 0.155 0.227 0.487 0.533 0.489 0.025 0.028 0.026

[29] 0.422 0.423 0.412 0.422 0.428 0.423 0.415 0.419 0.422 0.429 0.226 0.222 0.224 0.227 0.231 0.224 0.225 0.218 0.152 0.155 0.229 0.490 0.533 0.491 0.027 0.033 0.027 0.023

[30] 0.414 0.417 0.405 0.415 0.423 0.416 0.409 0.416 0.417 0.421 0.222 0.219 0.221 0.223 0.227 0.221 0.221 0.216 0.142 0.145 0.225 0.487 0.533 0.488 0.024 0.025 0.023 0.012 0.020

[31] 0.419 0.420 0.408 0.419 0.425 0.420 0.413 0.414 0.420 0.426 0.221 0.216 0.218 0.222 0.225 0.219 0.223 0.214 0.150 0.152 0.223 0.485 0.530 0.487 0.023 0.028 0.024 0.013 0.020 0.012

[32] 0.420 0.422 0.408 0.420 0.426 0.421 0.415 0.413 0.423 0.430 0.225 0.220 0.222 0.224 0.229 0.223 0.226 0.217 0.151 0.153 0.227 0.486 0.532 0.488 0.024 0.029 0.026 0.022 0.027 0.017 0.014

[33] 0.418 0.422 0.410 0.418 0.424 0.419 0.412 0.413 0.421 0.427 0.225 0.220 0.222 0.224 0.229 0.223 0.224 0.214 0.146 0.148 0.227 0.489 0.533 0.491 0.026 0.033 0.030 0.021 0.022 0.020 0.019 0.021

[34] 0.419 0.418 0.408 0.419 0.422 0.420 0.413 0.412 0.419 0.424 0.224 0.219 0.221 0.225 0.228 0.222 0.226 0.216 0.152 0.154 0.226 0.487 0.532 0.489 0.027 0.030 0.029 0.017 0.023 0.013 0.008 0.018 0.024

[35] 0.418 0.423 0.407 0.418 0.424 0.419 0.412 0.413 0.421 0.427 0.222 0.217 0.219 0.223 0.226 0.219 0.223 0.216 0.150 0.152 0.223 0.486 0.532 0.488 0.025 0.030 0.026 0.017 0.024 0.017 0.004 0.018 0.021 0.012

[36] 0.452 0.449 0.442 0.450 0.447 0.450 0.436 0.450 0.451 0.464 0.325 0.323 0.328 0.323 0.334 0.322 0.316 0.329 0.323 0.320 0.323 0.554 0.561 0.555 0.338 0.339 0.336 0.332 0.336 0.330 0.332 0.333 0.330 0.332 0.330

[37] 0.427 0.421 0.423 0.427 0.427 0.428 0.424 0.422 0.427 0.435 0.340 0.343 0.341 0.336 0.344 0.340 0.340 0.340 0.341 0.341 0.333 0.469 0.540 0.473 0.351 0.347 0.347 0.342 0.345 0.346 0.344 0.345 0.345 0.345 0.345 0.403

[38] 0.425 0.430 0.422 0.425 0.434 0.426 0.423 0.425 0.436 0.451 0.391 0.390 0.394 0.392 0.397 0.391 0.390 0.389 0.371 0.371 0.389 0.502 0.570 0.498 0.382 0.381 0.381 0.381 0.383 0.381 0.380 0.379 0.380 0.381 0.380 0.415 0.326

[39] 0.393 0.407 0.394 0.393 0.402 0.394 0.394 0.397 0.404 0.413 0.371 0.372 0.370 0.368 0.376 0.369 0.366 0.375 0.362 0.362 0.370 0.494 0.573 0.496 0.370 0.369 0.370 0.365 0.369 0.369 0.364 0.366 0.367 0.365 0.363 0.403 0.286 0.332

within type comparison, between types/within species comparison,

between species/within genus comparison, between genera comparison