This form should be used for all taxonomic proposals. Please complete all those modules that are applicable (and then delete the unwanted sections). For guidance, see the notes written in blue and the separate document "Help with completing a taxonomic proposal"

Please try to keep related proposals within a single document; you can copy the modules to create more than one genus within a new family, for example.

MODULE 1: **TITLE, AUTHORS, etc**

Code assigned:	***2013.004aV***	(to be completed by ICTV officers)

Short title:
Create species *SFTS virus* in the genus *Phlebovirus*, family *Bunyaviridae*

(e.g. 6 new species in the genus *Zetavirus*)

Modules attached (modules 1 and 9 are required)	**1** ☒	**2** ☒	**3** ☐	**4** ☐	**5** ☐
	6 ☐	**7** ☐	**8** ☐	**9** ☒	

Author(s) with e-mail address(es) of the proposer:

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Mifang Liang (mifangl@vip.sina.com)

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 (fungal, invertebrate, plant, prokaryote or vertebrate viruses)	*Bunyaviridae* Study Group

ICTV-EC or Study Group comments and response of the proposer:

Date first submitted to ICTV:	20120912
Date of this revision (if different to above):	20130616

MODULE 2: **NEW SPECIES**

creating and naming one or more new species.

If more than one, they should be a group of related species belonging to the same genus. All new species must be placed in a higher taxon. This is usually a genus although it is also permissible for species to be "unassigned" within a subfamily or family. Wherever possible, provide sequence accession number(s) for one isolate of each new species proposed.

Code	***2014.005aV***	(assigned by ICTV officers)

To create one new species within:

Genus:	***Phlebovirus***
Subfamily:	**Unassigned**
Family:	***Bunyaviridae***
Order:	**Unassigned**

Fill in all that apply.
- If the higher taxon has yet to be created (in a later module, below) write "**(new)**" after its proposed name.
- If no genus is specified, enter "**unassigned**" in the genus box.

And name the new species:	**GenBank sequence accession number(s) of reference isolate:**
SFTS virus	Sequences are available for three genomic segments of *SFTS virus*, Strain HB29. L segment: (HM745930) M segment: (HM745931) S segment: (HM745932) More see table 1.

Reasons to justify the creation and assignment of the new species:

- Explain how the proposed species differ(s) from all existing species.
  - If species demarcation criteria (see module 3) have previously been defined for the genus, **explain how the new species meet these criteria**.
  - If criteria for demarcating species need to be defined (because there will now be more than one species in the genus), please state the proposed criteria.
- Further material in support of this proposal may be presented in the Appendix, Module 9

The proposed novel species *SFTS virus*, initially designated as Severe fever with thrombocytopenia syndrome bunyavirus (SFTSV) [1], is a novel virus newly identified to cause severe fever with thrombocytopenia syndrome (SFTS) in China. The common clinical presentation of SFTS includes high fever, gastrointestinal symptoms, thrombocytopenia, leukocytopenia, and multi-organ dysfunction with an initial case fatality rate of 30% . SFTS has been reported in at least 13 provinces in the Central, Eastern, and Northeastern regions of China, also in USA [12]., Japan and Korea [personal communications).

SFTSV first emerged in six provinces of Hubei, Shandong, Henan, Jiangsu, Anhui

and Liaoning, located in central and north-east China, in 2009 and 2010. A total of 12 SFTSV strains were initially isolated from SFTS patients from 6 provinces in China (Table 1). SFTSV was first reported as the causing pathogen of SFTS in 2011 [1]. Following the initial outbreak, surveillance studies identified SFTSV as more broadly distributed. More viral isolates were obtained from SFTS patients [1-6], domestic animals (sheep, cattle and dog) and ticks, which suggested the potential vectors and animal hosts [7, 8]. The recent discovery of human-to-human transmission indicated the potential threats for public health [2-3]. In addition, high seroprevalence of viral antibodies were detected from sheep, cattle, dogs, chickens and pigs in the endemic areas in China, which demonstrated SFTSV has wide host range in nature [5, 7-10]

SFTSV can infect a variety of cells including Vero and macrophage cells (DH82, THP-1 cells) [1, 11]. Negative-stain electron microscopy revealed that virus particles are spheres with diameters of 80-100 nm, a similar morphology to bunyavirus particles (Figure 1).

Like other members of the genus *Phlebovirus* , family *Bunyaviridae*, SFTSV is an enveloped, negative stranded RNA virus with three single-stranded RNA genome consisting of large (L), medium (M), and small (S) segments [1]. The L and M segments are of negative polarity. The L segment contains 6368 nucleotides with one open reading frame encoding RNA dependent RNA polymerase (RdRP) composed of 2084 amino acids. The M segment contains 3378 nucleotides with one open reading frame encoding 1073 amino acid precursor of glycoproteins Gn and Gc. The S segment of the virus contains 1744 nucleotides, which uses an ambisense strategy to encode for the nucleoprotein (N) in antisense orientation and for the nonstructural protein (NSs) in sense orientation, separated by a 54-bp intergenic region (Figure 2). The 5' and 3' terminus of L, M and S segments possess short noncoding sequences , The 5’ noncoding regions of SFTSV (strain HB29) are 16 nt (L), 18nt (M) and 42nt (S); and the 3’ noncoding regions are 100nt (L), 141nt (M) and 28nt (S).

Phylogenetic analyses based on complete viral genomic sequence of L, M and S segments from a panel of SFTSV strains isolated from SFTS patients, showed that the novel virus was classified into the genus *Phlebovirus,* family *Bunyaviridae* (Figure

3A and 3B). Further, phylogenetic analysis of complete deduced amino acid sequences for RdRP, glycoprotein (Gn and Gc), N and NSs proteins of 8 SFTSV strains, including strains HB29 and 5 other strains [1], Huaiyangshan [5] and Henan Fever [6], showed that all SFTSV isolates clustered together in comparison to other known phleboviruses, but were almost equally distant from the Sandfly fever group and the Uukuniemi group (Figure 4). These results suggest that *SFTS virus* is a novel species of the genus *Phlebovirus*. In comparison with the recent discovered *Heartland virus* [12], *SFTS virus* is classified in a distinct lineage although *Heartland virus* is closer than other phleboviruses (Figure 3 and Figure 4). The comparison of amino acid sequence similarity provided further support to the separation of *SFTS virus* from other phleboviruses (Table 2). Both RdRp and glycoprotein (Gn and Gc) of SFTSV are slightly more closely related to counterparts in Uukuniemi virus but only share maximum 36% similarity, while the most conserved N protein of SFTSV only shared 41% similarity with Rift Valley fever virus. With more diversity, the S segment encoded NSs protein of SFTSV showed the lowest amino acid similarity of only 11-16.0%. The high diversity of SFTSV with other phleboviruses suggested that *SFTS virus* is a novel species in the genus *Phlebovirus*.

Serological comparisons of the antigenic character of SFTSV with other phleboviruses were carried out by cross reaction of SFTS patients sera with recombinant N proteins from selected phleboviruses using indirect IgG ELISA. The results showed that no serological cross reactions were found between SFTSV and the selected phleboviruses, including Rift Valley fever virus (RVFV), Heartland virus (HLV), Uukuniemi virus(UUKV), Sandfly fever Naples virus (SFNV) and Sandfly fever Sicilian virus (SFSV) (Table 3), indicated SFTSV belongs to a new serological group in the genus *Phlebovirus*.

In conclusion, *SFTS virus* is a new species of the genus *Phlebovirus,* family *Bunyaviridae.*

MODULE 9: **APPENDIX**: supporting material

additional material in support of this proposal

References:

1. Yu, X.J., et al., *Fever with thrombocytopenia associated with a novel bunyavirus in China.* N Engl J Med, 2011. 364(16): p. 1523-32.
2. Gai, Z., et al., *Person-to-person transmission of severe fever with thrombocytopenia syndrome bunyavirus through blood contact.* Clin Infect Dis, 2012. 54(2): p. 249-52.
3. Bao,C.J., et al., *A family cluster of infections by a newly recognized bunyavirus in eastern China, 2007: further evidence of person-to-person transmission.* Clin Infect Dis, 2011. 53(12): p. 1208-14
4. Dexin Li , *Correspondence letter, A novel bunyavirus in China.* N Engl J Med, 2011. 365(9): 864-5.
5. Zhang, Y.Z., et al., *The ecology, genetic diversity, and phylogeny of Huaiyangshan virus in China.* J Virol, 2012. 86(5): p. 2864-8.
6. Xu, B., et al., *Metagenomic analysis of fever, thrombocytopenia and leukopenia syndrome (FTLS) in Henan Province, China: discovery of a new bunyavirus.* PLoS Pathog, 2011. 7(11): p. e1002369.
7. Niu, G., et al., *Infection of severe fever with thrombocytopenia syndrome virus in domesticated animals, China.* Emerg Infect Dis. 2013, 19(5): p. 756–763. http://dx.doi.org/10.3201/eid1905.120245
8. Jiang XL, et al. *Isolation, identification and characterization of SFTS bunyavirus from ticks collected on the surface of domestic animals* [in Chinese]. Chinese J Virol. 2012, 28(3):252-7.
9. Jiao, Y., et al., *Preparation and evaluation of recombinant severe fever with thrombocytopenia syndrome virus nucleocapsid protein for detection of total antibodies in human and animal sera by double-antigen sandwich enzyme-linked immunosorbent assay.* J Clin Microbiol, 2012. 50(2): p. 372-7.
10. Zhao, L., et al., *Severe fever with thrombocytopenia syndrome virus, Shandong Province, China.* Emerg Infect Dis, 2012. 18(6): p. 963-5.
11. Jin, C., et al., *Pathogenesis of emerging severe fever with thrombocytopenia syndrome virus in C57/BL6 mouse model.* Proc Natl Acad Sci U S A, 2012. 109(25): p. 10053-8.
12. McMullan L.K., et al., *A new phlebovirus associated with severe febrile illness in Missouri.* N Engl J Med, 2012. 367(9): p.834-41.

Annex:

Include as much information as necessary to support the proposal, including diagrams comparing the old and new taxonomic orders. The use of Figures and Tables is strongly recommended but direct pasting of content from publications will require permission from the copyright holder together with appropriate acknowledgement as this proposal will be placed on a public web site. For phylogenetic analysis, try to provide a tree where branch length is related to genetic distance.

Table 1. GenBank numbers of complete genomic sequences of new SFTSV isolates

SFTSV isolates	Genome segments		
	L	M	S
HB29	HM745930	HM745931	HM745932
SD4	HM802202	HM802203	HM802204
SD24	HM802200	HM802201	HM802205
AH12	HQ116417	HQ141590	HQ141591
AH15	HQ141592	HQ141593	HQ141594
DMB*	HM160499	HQ655878	HM160498
HN6	HQ141595	HQ141596	HQ141597
HN13	HQ141598	HQ141599	HQ141600
JS3	HQ141601	HQ141602	HQ141603
JS4	HQ141604	HQ141605	HQ141606
LN2	HQ141607	HQ141608	HQ141609
LN3	HQ141610	HQ141611	HQ141612

*Partial sequences

Table 2. Amino acid sequence similarity (%) comparison between *SFTS virus* and representative phleboviruses

Proteins	Strains	*RVFV/ 74HB59	Massila /W	PTV/ Adames	SFV/ Sicilian	Toscana/AR	UUK/ S23	SFTS/ HB29
RdRp	RVF/74HB59	100.0	54.4	***	***	54.4	37.2	33.0
	Massila/W		100.0			83.3	36.0	32.2
	Toscana/AR					100.0	36.0	31.9
	UUK/S23						100.0	33.1
	SFTSV/HB29							100.0
Gn+Gc	RVF/74HB59	100.0	35.1	40.5	38.9	36.2	30.9	30.8
	Massila/W		100.0	33.8	31.6	57.6	21.8	21.4
	PTV/Adames			100.0	38.3	33.1	23.4	23.1
	SFV/Sicilian/				100.0	31.5	22.0	21.4
	Toscana/AR					100.0	22.3	19.8
	UUK/S23						100.0	36.1
	SFTSV/HB29							100.0
N	RVF/74HB59	100.0	49.6	56.1	53.8	50.0	37.1	41.4
	Massila/W		100.0	50.6	43.8	85.4	30.8	35.1
	PTV/Adames			100.0	50.0	52.6	35.7	38.2
	SFV / Sicilian				100.0	43.8	34.7	38.5
	Toscana/AR					100.0	29.2	34.3
	UUK/S23						100.0	29.5
	SFTSV/HB29							100.0
NSs	RVF/74HB59	100.0	16.0	21.8	26.8	17.7	9.3	11.5
	Massila/W		100.0	12.6	14.7	45.9	8.6	16.0
	PTV/Adames			100.0	21.6	13.4	9.7	11.8
	SFV/ Sicilian				100.0	17.6	11.9	11.2
	Toscana/AR					100.0	9.4	14.9
	UUK/S23						100.0	13.7
	SFTSV/HB29							100.0

*RVF: *Rift valley fever virus*; PTV: *Punta Toro virus*; SFV: *Sandfly fever virus*: UUK: *Uukuniemi virus*; SFTSV: *SFTS virus*

Figure 1. Morphologic Features of negatively stained SFTSV virions purified from SFTSV-infected Vero cells.

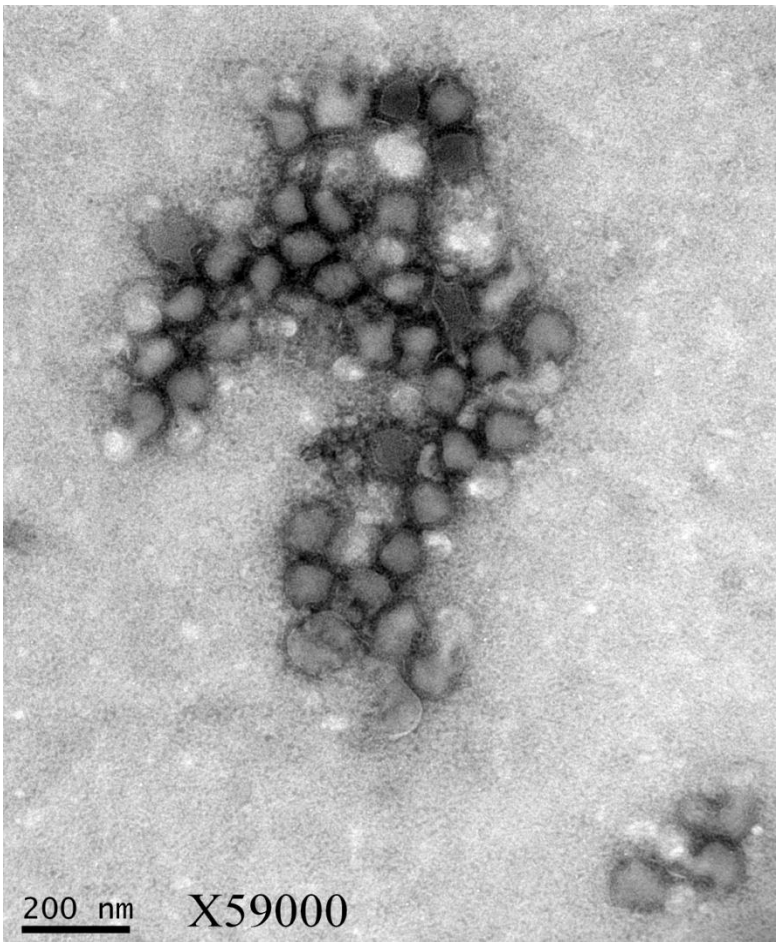


Figure 2. Genomic structure and coding strategies of SFTSV

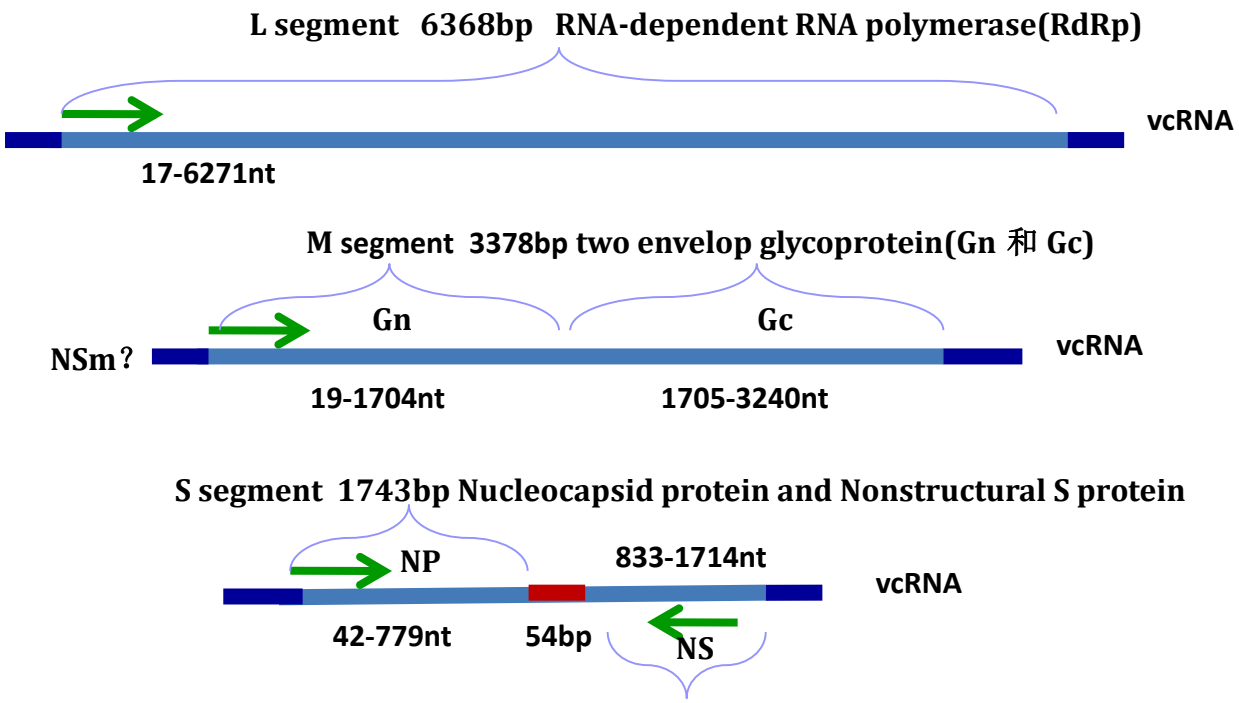
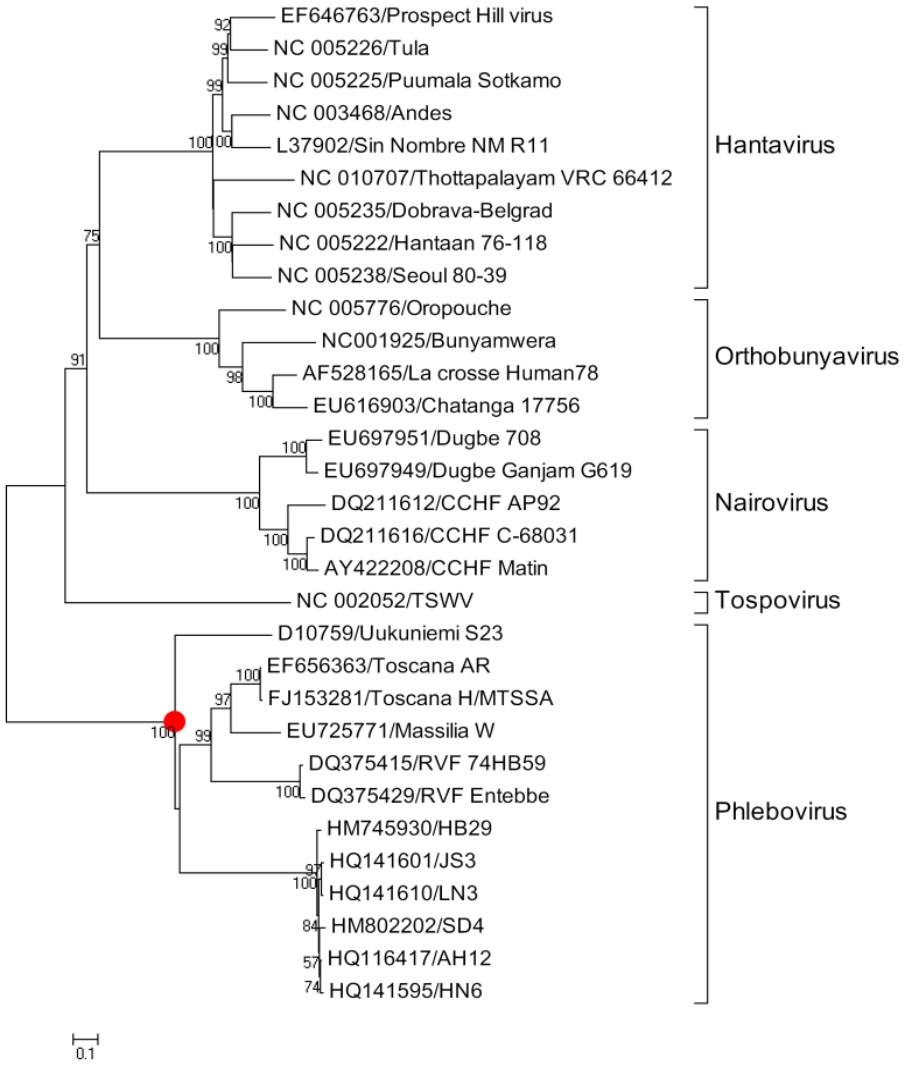


Figure 3A. Phylogenetic analysis of *SFTS virus* with representative members of the family *Bunyaviridae* Sequences from L, M and S segments of SFTSV were aligned with MEGA4. Trees were generated using neighbor-joining method with the use of Poisson correction and complete deletion of gaps. Branch lengths are proportional to evolutionary distance (scale bar). Bootstrap testing (2000 replicates) was performed, and the bootstrap values are indicated. Sequences are identified by their GenBank accession numbers, followed by the virus name and strain. The red dot indicates the phlebovirus cluster.

L segments



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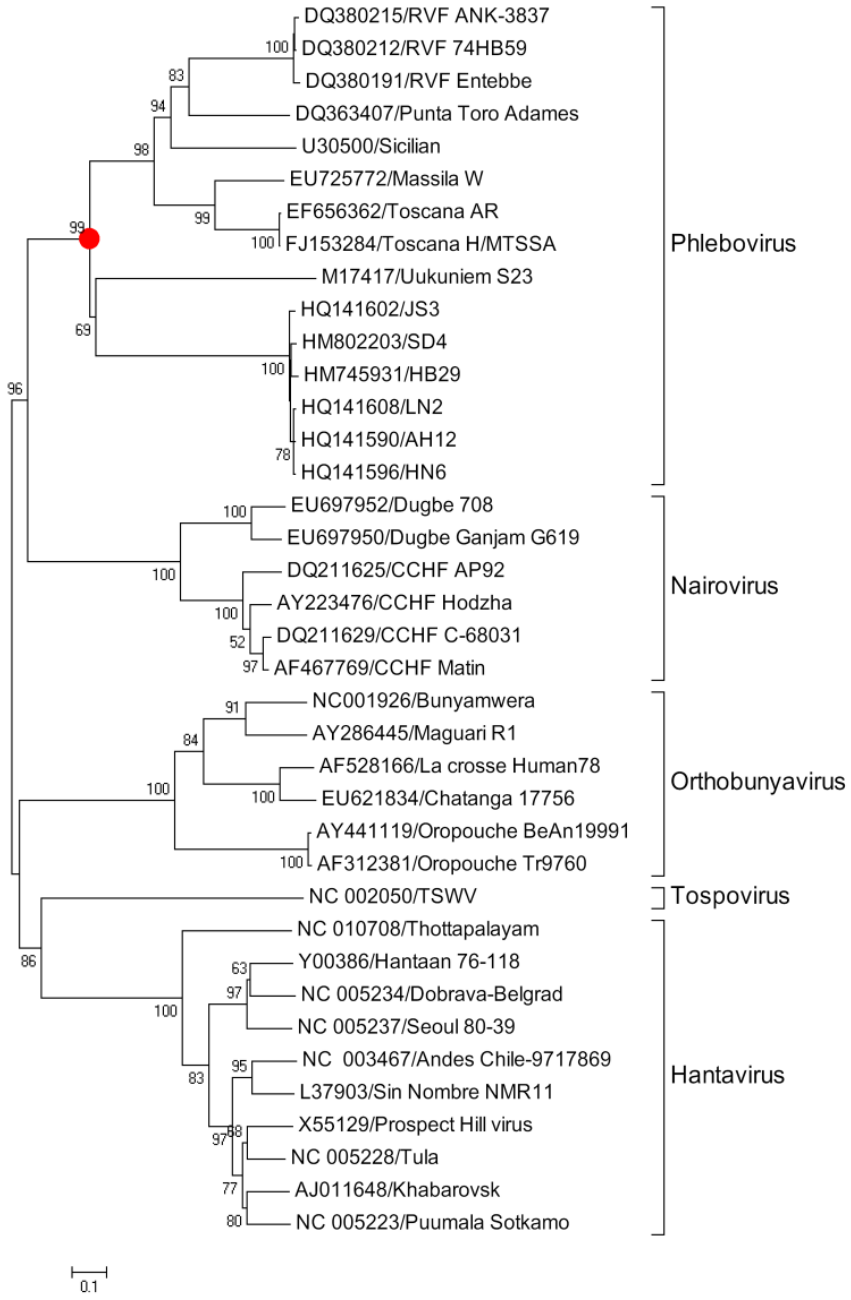
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DQ380191/RVF Entebbe
DQ363407/Punta Toro Adames
U30500/Sicilian
EU725772/Massila W
EF656362/Toscana AR
FJ153284/Toscana H/MTSSA
M17417/Uukuniem S23
HQ141602/JS3
HM802203/SD4
HM745931/HB29
HQ141608/LN2
HQ141590/AH12
HQ141596/HN6
Phlebovirus
EU697952/Dugbe 708
EU697950/Dugbe Ganjam G619
DQ211625/CCHF AP92
AY223476/CCHF Hodzha
DQ211629/CCHF C-68031
AF467769/CCHF Matin
Nairovirus
NC001926/Bunyamwera
AY286445/Maguari R1
AF528166/La crosse Human78
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AY441119/Oropouche BeAn19991
AF312381/Oropouche Tr9760
Orthobunyavirus
NC 002050/TSWV
Tospovirus
NC 010708/Thottapalayam
Y00386/Hantaan 76-118
NC 005234/Dobrava-Belgrad
NC 005237/Seoul 80-39
NC 003467/Andes Chile-9717869
L37903/Sin Nombre NMR11
X55129/Prospect Hill virus
NC 005228/Tula
AJ011648/Khabarovsk
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Hantavirus
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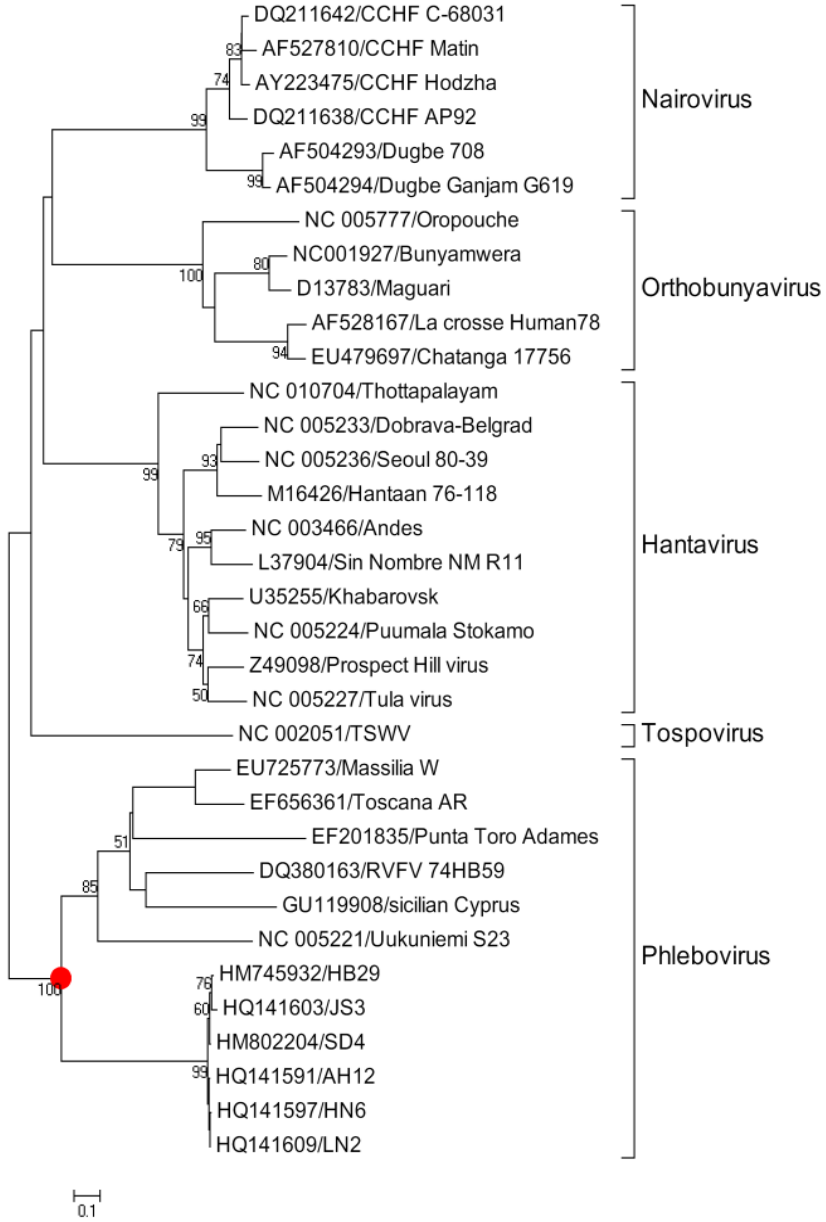
S segments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Nairovirus
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NC001927/Bunyamwera
D13783/Maguari
AF528167/La crosse Human78
EU479697/Chatanga 17756
Orthobunyavirus
NC 010704/Thottapalayam
NC 005233/Dobrava-Belgrad
NC 005236/Seoul 80-39
M16426/Hantaan 76-118
NC 003466/Andes
L37904/Sin Nombre NM R11
U35255/Khabarovsk
NC 005224/Puumala Stokamo
Z49098/Prospect Hill virus
NC 005227/Tula virus
Hantavirus
NC 002051/TSWV
Tospovirus
EU725773/Massilia W
EF656361/Toscana AR
EF201835/Punta Toro Adames
DQ380163/RVFV 74HB59
GU119908/sicilian Cyprus
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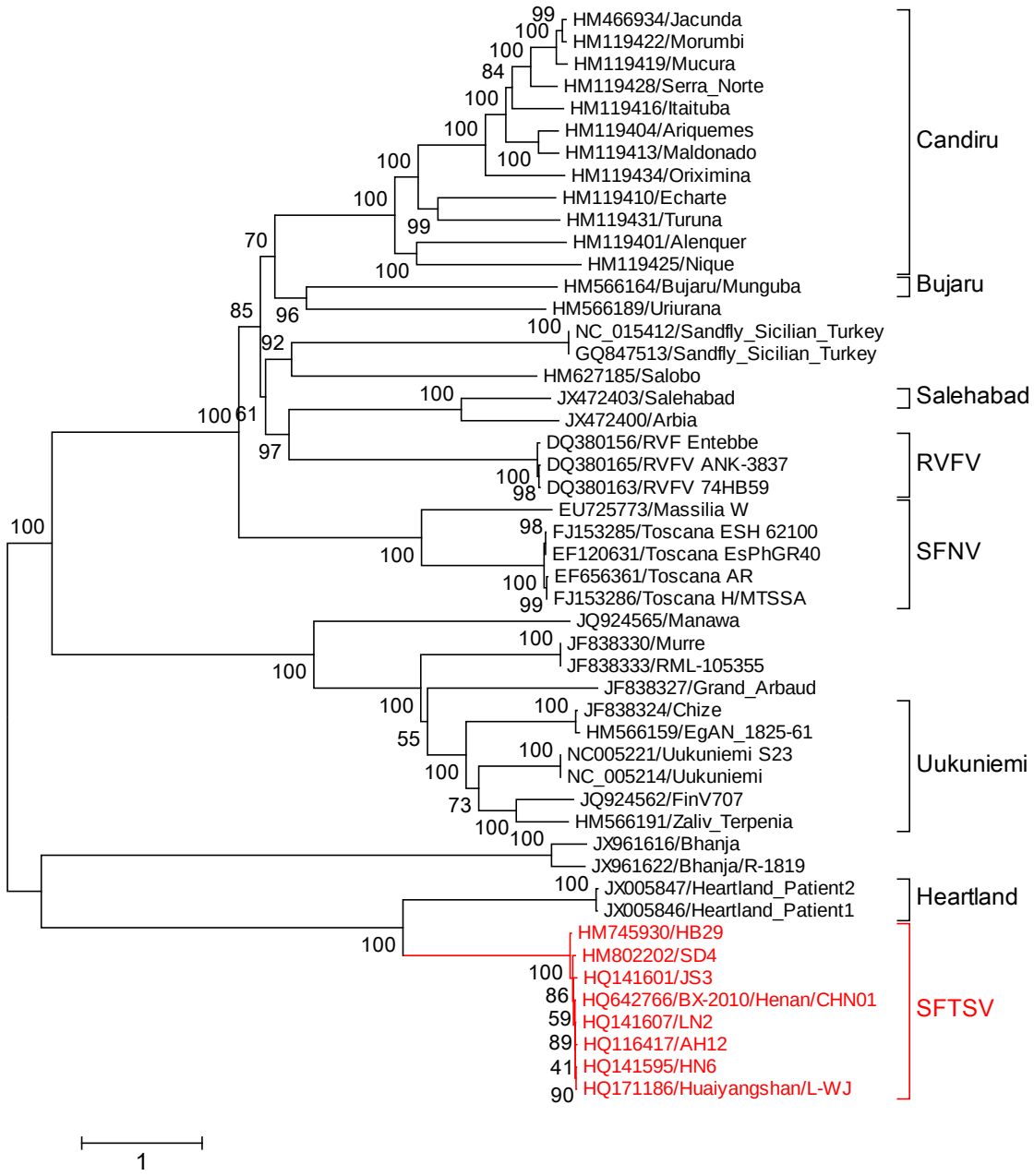
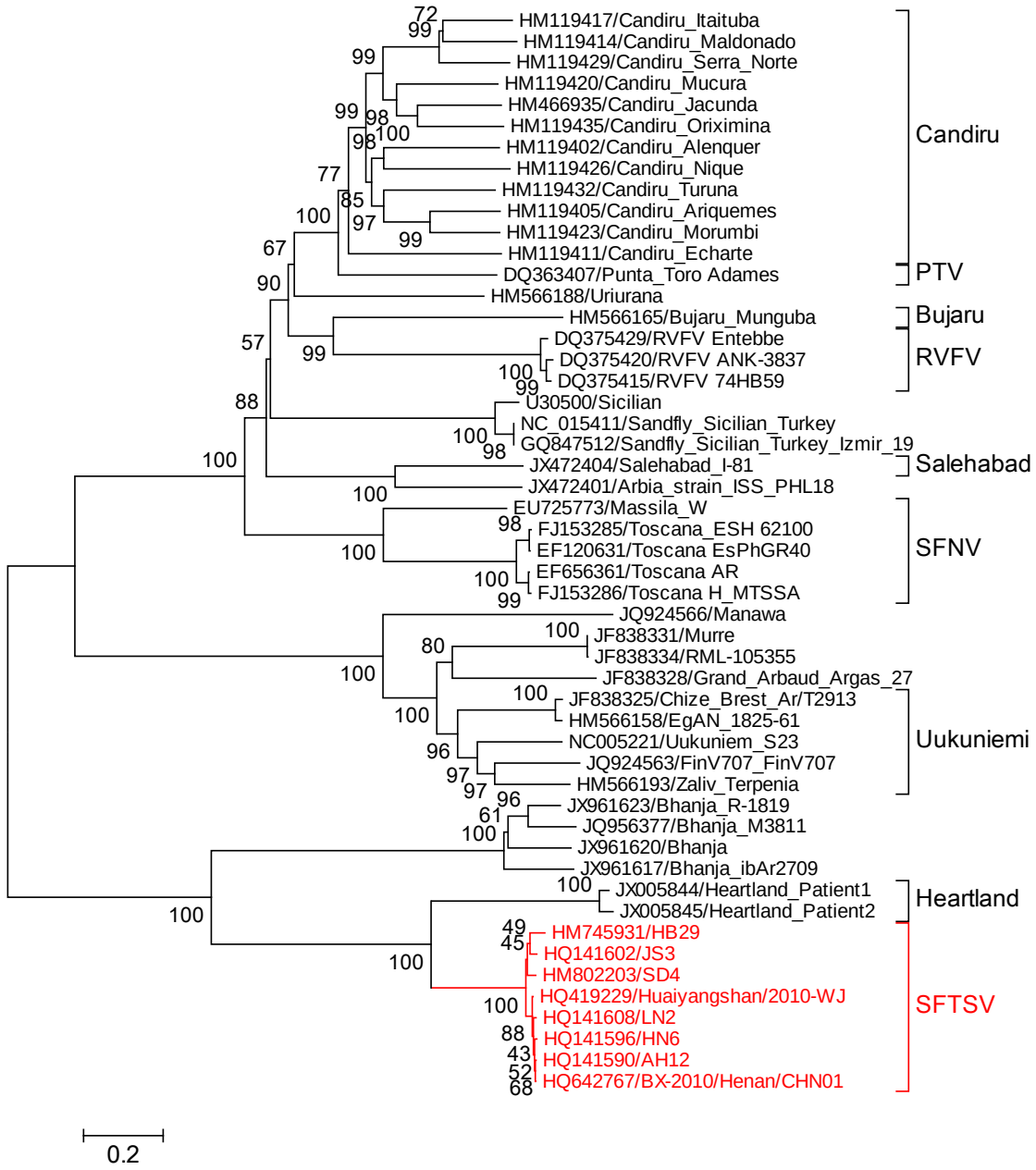
HM745932/HB29
HQ141603/JS3
HM802204/SD4
HQ141591/AH12
HQ141597/HN6
HQ141609/LN2
Phlebovirus
0.1

Figure 3B. Phylogenetic analysis of SFTSV with members in the genus of *Phlebovirus*. Sequences from L, M and S segments of SFTSV were aligned with MEGA4. Trees were generated using neighbor-joining method with the use of Poisson correction and complete deletion of gaps. Branch lengths are proportional to evolutionary distance (scale bar). Bootstrap testing (2000 replicates) was performed, and the bootstrap values are indicated. Sequences are identified by their GenBank accession numbers, followed by the virus name and strain. The red color indicate SFTSV clusters.

L segments



M segments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HM119435/Candiru_Oriximina
HM119402/Candiru_Alenquer
HM119426/Candiru_Nique
HM119432/Candiru_Turuna
HM119405/Candiru_Ariquemes
HM119423/Candiru_Morumbi
HM119411/Candiru_Echarte
Candiru
DQ363407/Punta_Toro Adames
PTV
HM566188/Uriurana
HM566165/Bujaru_Munguba
Bujaru
DQ375429/RVFV Entebbe
DQ375420/RVFV ANK-3837
DQ375415/RVFV 74HB59
RVFV
U30500/Sicilian
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EF120631/Toscana EsPhGR40
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HM802203/SD4
HQ419229/Huaiyangshan/2010-WJ
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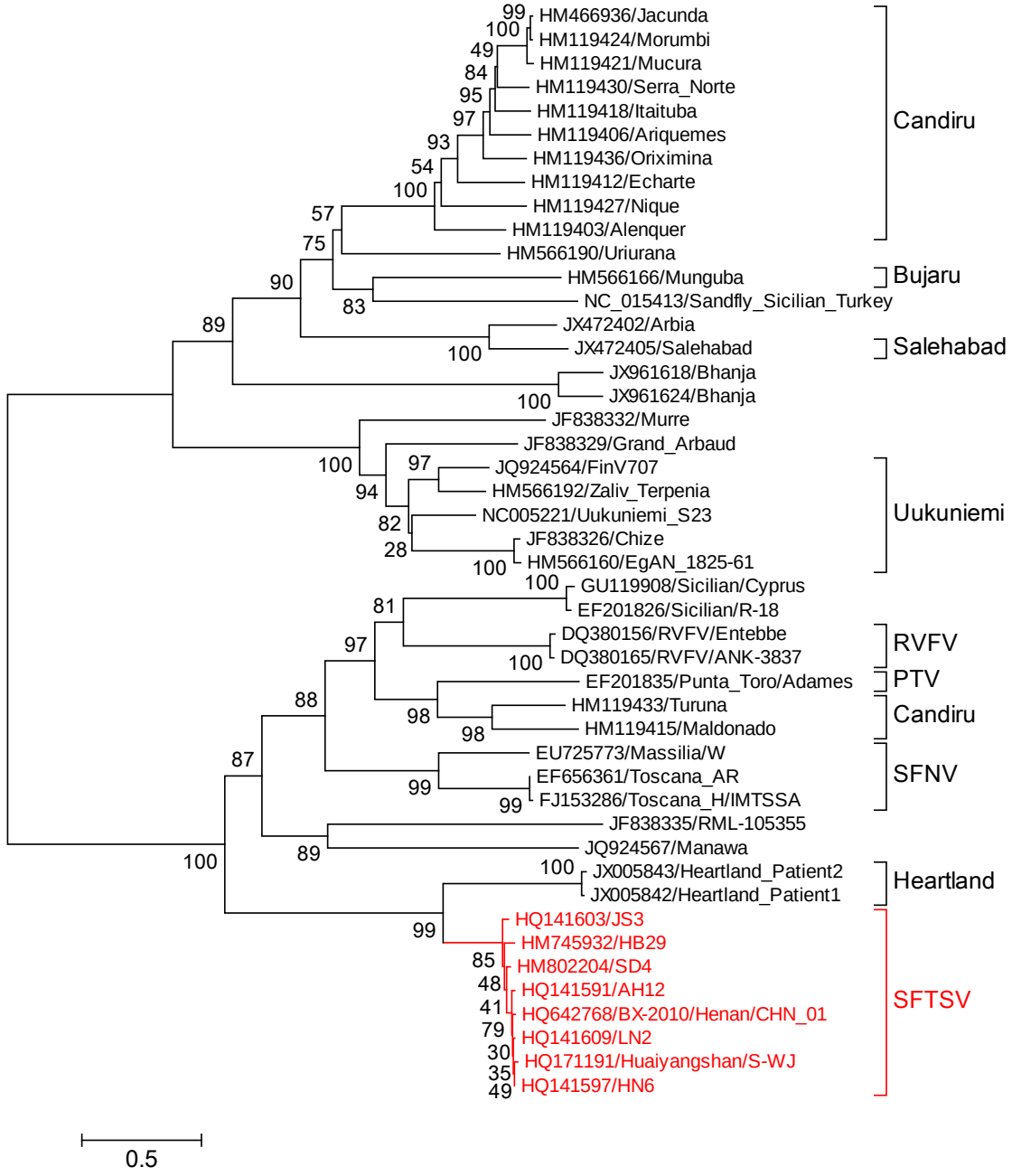
SFTSV
0.2

S segments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HM802204/SD4
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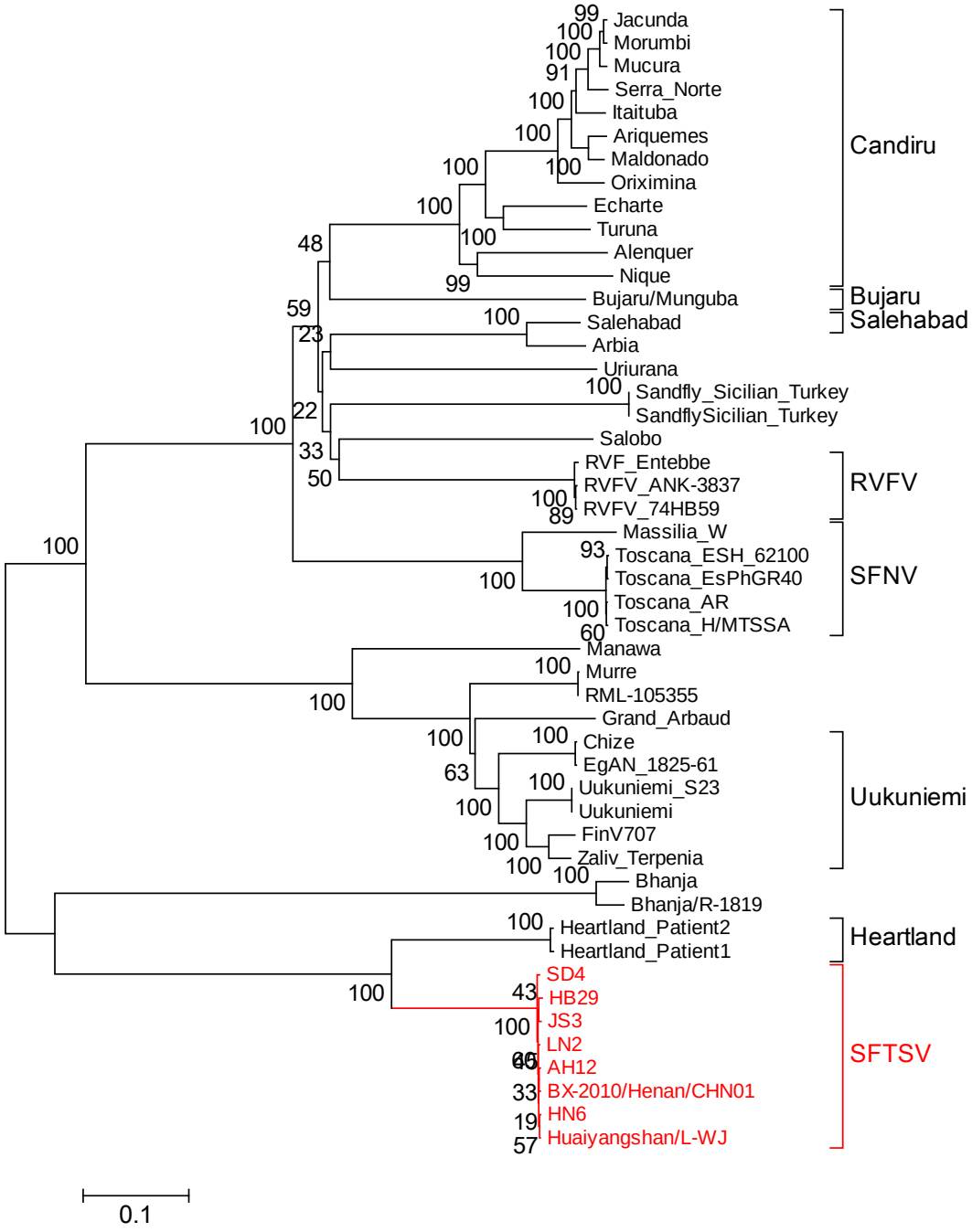
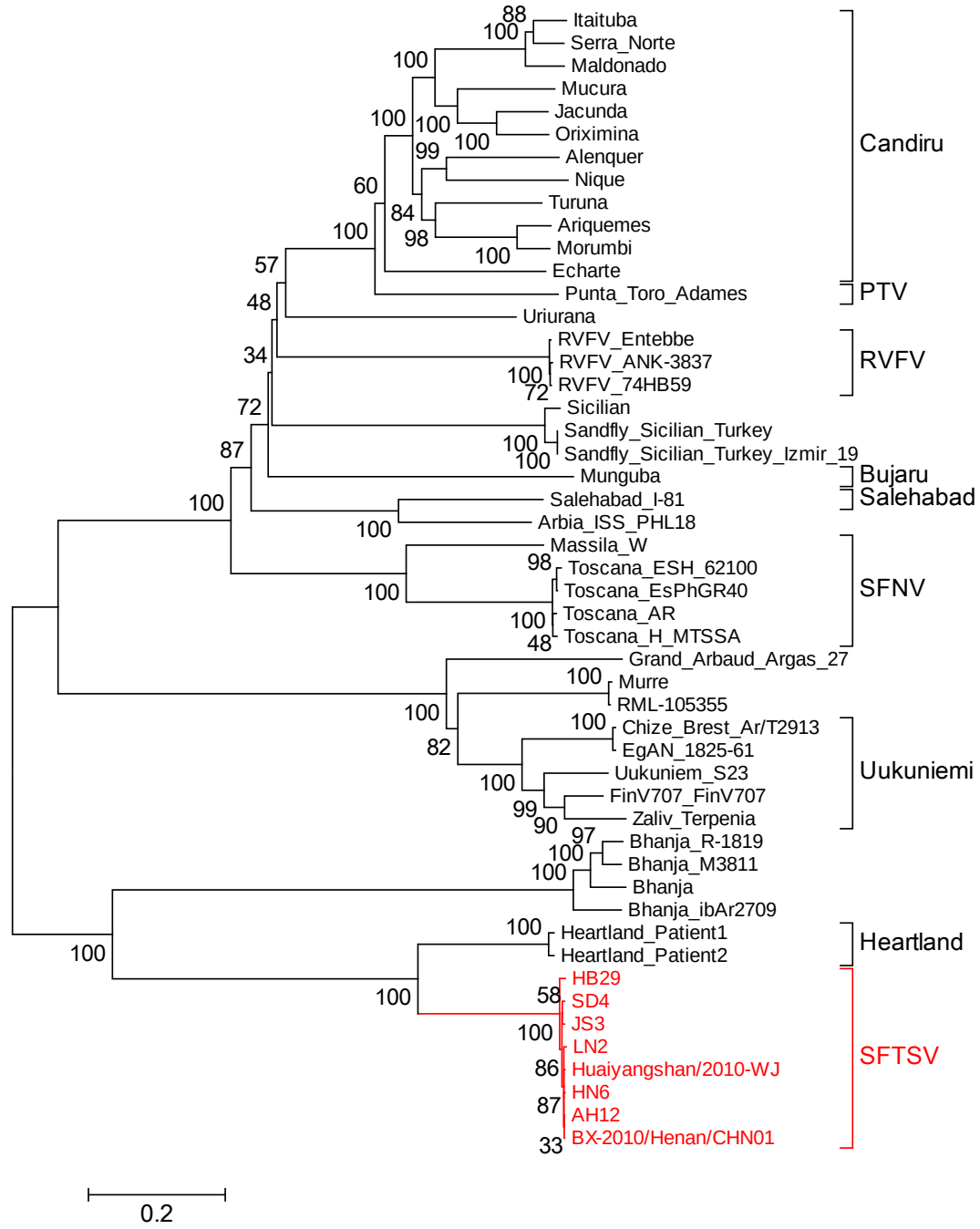
HQ141609/LN2
HQ171191/Huaiyangshan/S-WJ
HQ141597/HN6
Candiru
Bujaru
Salehabad
Uukuniemi
RVFV
PTV
Candiru
SFNV
Heartland
SFTSV
0.5

Figure 4. Phylogenetic analyses of SFTV structural and non-structural proteins. Amino acid sequences were aligned with MEGA4. Trees were generated using neighbor-joining method with the use of Poisson correction and complete deletion of gaps. Branch lengths are proportional to evolutionary distance (scale bar). Bootstrap testing (2000 replicates) was performed, and the bootstrap values are indicated.S equences are identified by their GenBank accession numbers, followed by the virus name and strain. The red color indicates the cluster of SFTSV strains.

RdRP



GP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Echarte
Candiru
Punta_Toro_Adames
PTV
Uriurana
RVFV_Entebbe
RVFV_ANK-3837
RVFV_74HB59
RVFV
Sicilian
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Bhanja
Bhanja_ibAr2709
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Heartland_Patient2
Heartland
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SD4
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HN6
AH12
BX-2010/Henan/CHN01
SFTSV
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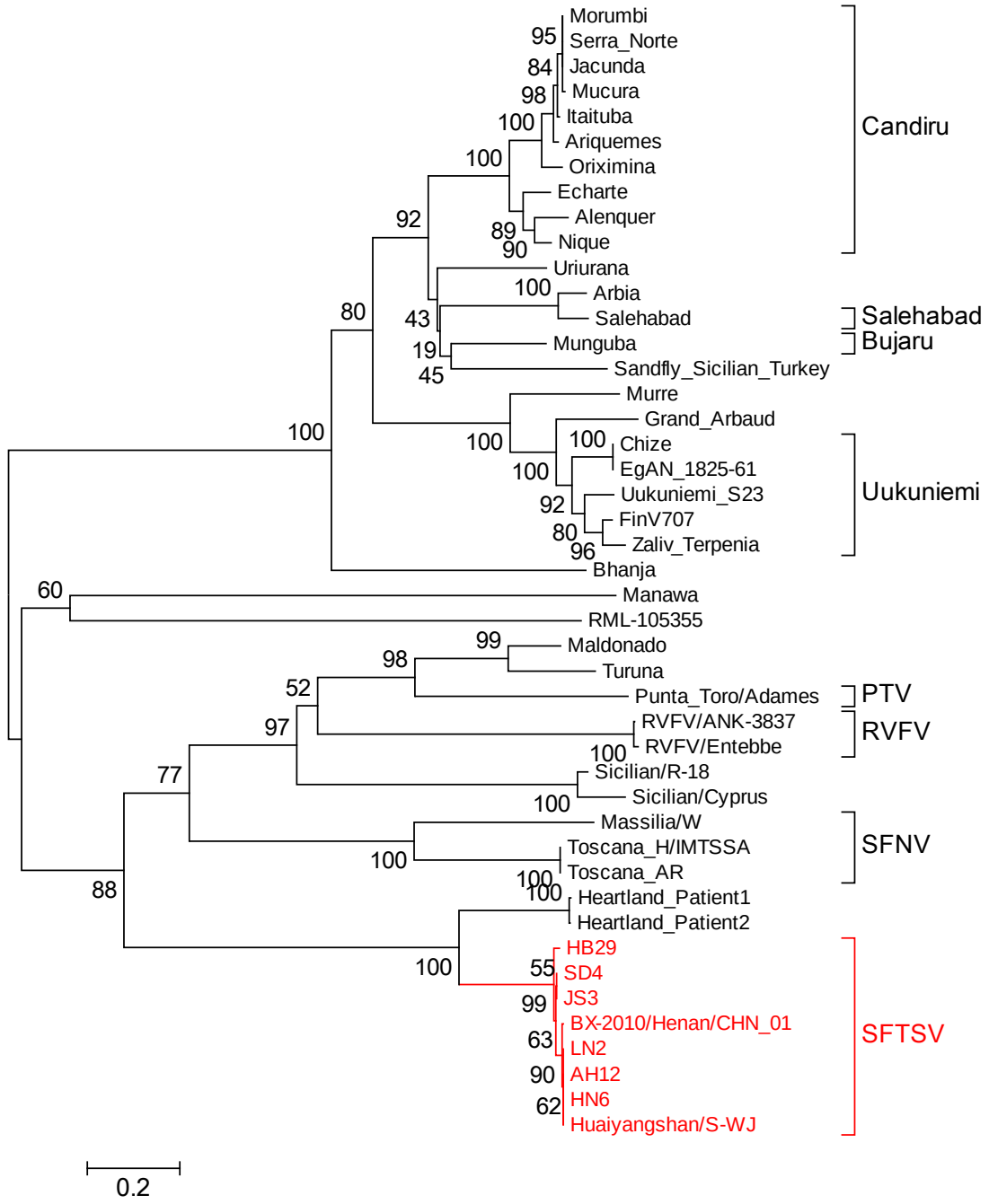
NP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Munguba
Sandfly_Sicilian_Turkey
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Turuna
Punta_Toro/Adames
RVFV/ANK-3837
RVFV/Entebbe
Sicilian/R-18
Sicilian/Cyprus
Massilia/W
Toscana_H/IMTSSA
Toscana_AR
Heartland_Patient1
Heartland_Patient2
HB29
SD4
JS3
BX-2010/Henan/CHN_01
LN2
AH12
HN6
Huaiyangshan/S-WJ
Candiru
Salehabad
Bujaru
Uukuniemi
PTV
RVFV
SFNV
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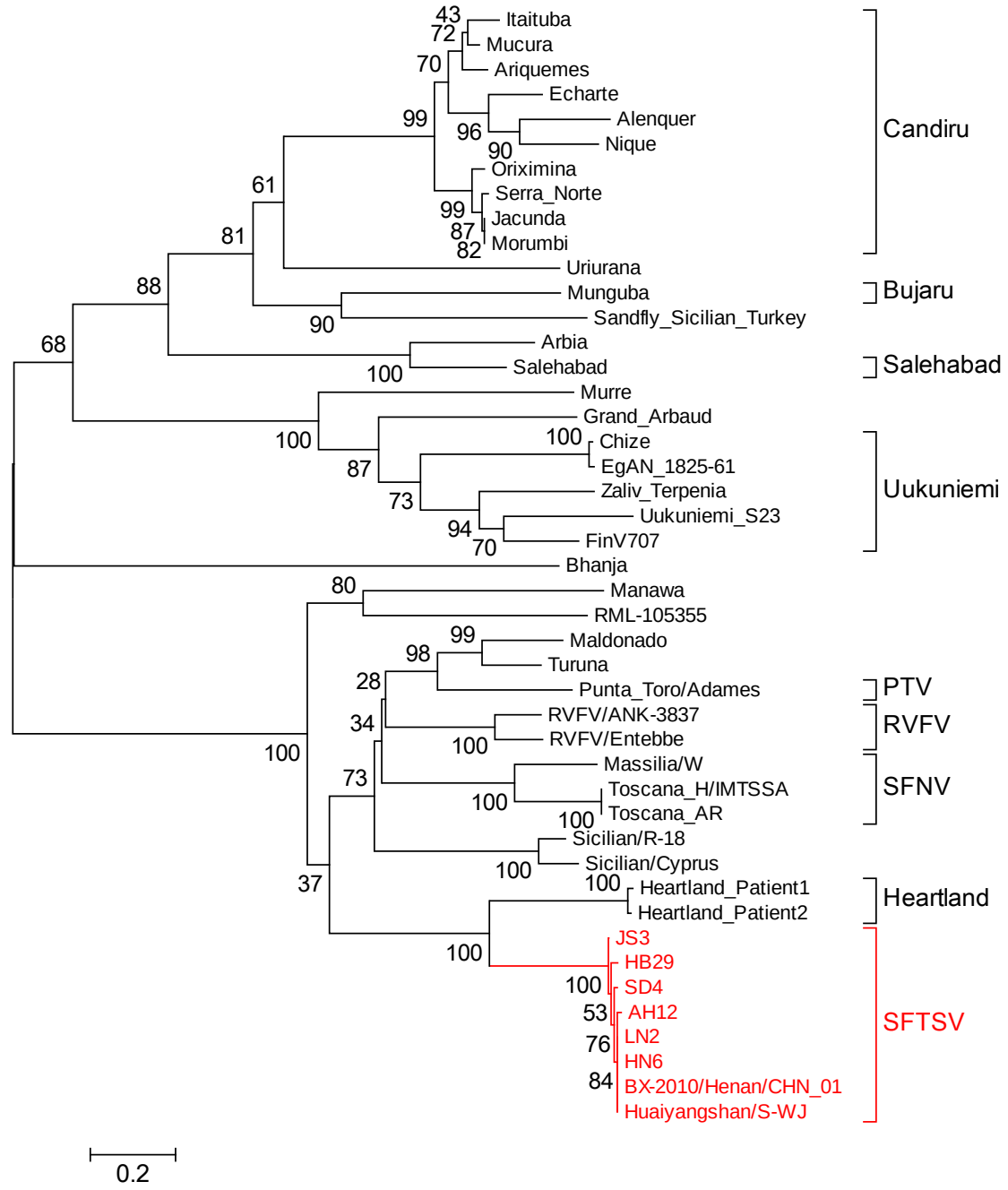
NSs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Heartland
SFTSV
0.2

Table3 Cross reaction of SFTS patients sera with N proteins from selected phleboviruses using indirect IgG ELISA

Serum	Antigen*					
	RVFV-N	SFTSV-N	HLV-N	UUKV-N	SFNV-N	SFSV-N
SFTS Patient1	<100	12800	200	<100	<100	<100
SFTS Patient2	100	25600	200	<100	<100	<100
SFTS Patient3	<100	25600	<100	<100	<100	<100
SFTS Patient4	100	51200	200	<100	<100	<100
SFTS Patient5	<100	12800	<100	<100	<100	<100
SFTS Patient6	<100	1600	200	<100	<100	<100
SFTS Patient7	<100	6400	200	<100	<100	<100
SFTS Patient8	<100	25600	<100	<100	<100	<100
SFTS Patient9	<100	800	<100	<100	<100	<100
SFTS Patient10	<100	12800	<100	<100	<100	<100

* Recombinant nucleocapsid protein antigen was produced in E.*coli*. RVFV: *Rift Valley fever virus*; HLV: *Heartland virus*; UUKV: *Uukuniemi virus*; SFNV: *Sandfly fever Naples virus*; SFSV: Sandfly fever Sicilian virus.