Supplementary Material

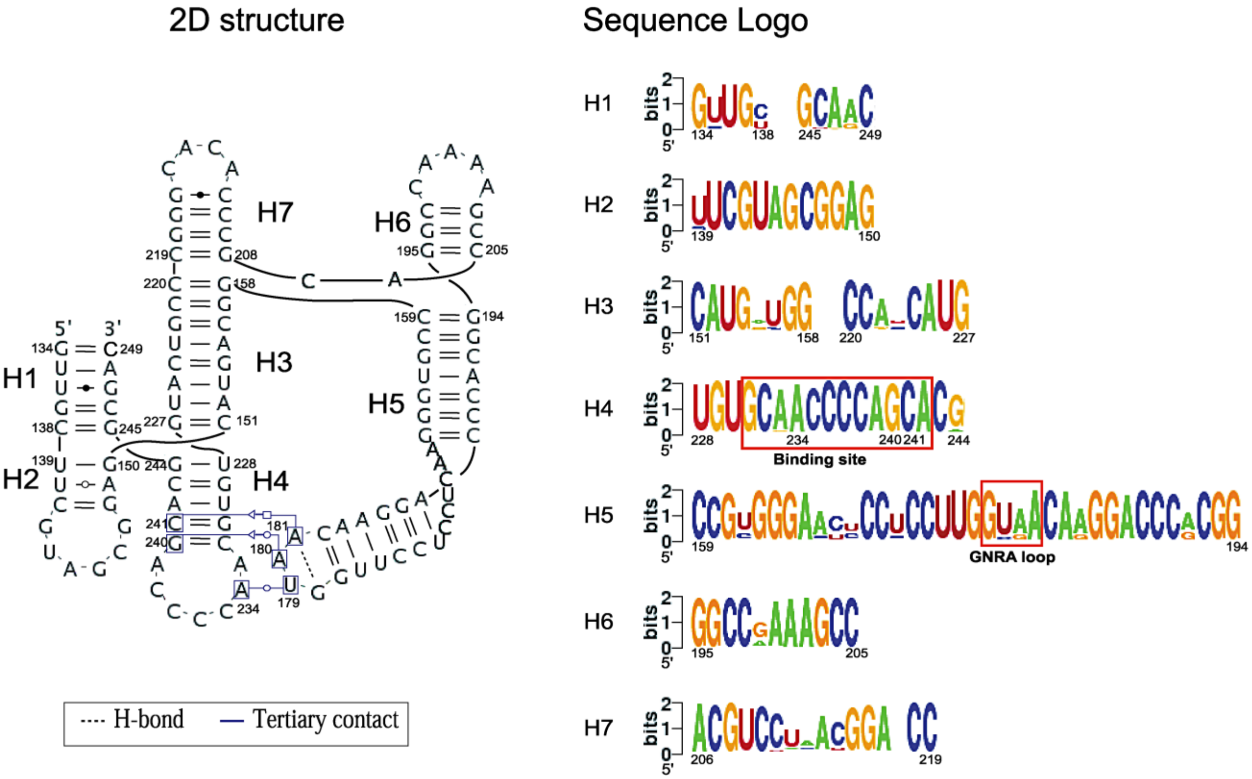

Figure S1. Sequence conservation analysis using logo for sequences of the apical region in domain 3 derived from 318 FMDV IRES systems listed in Table S2. The RNA sequence consists of four letters (bases) —A, U, G, and C, and the sequence logos consist of a stack of the four letters quantified by 2 bits (1 bit can describe two possible values) at each position in a sequence. The 2 bit high vertical bar is a measure of the relative frequency of the four letters. While the overall height of a stack indicates a degree of sequence conservation, the height of each letter within the stack shows the relative frequency at each position. At each nucleotide position, most to least frequent bases are placed from top to bottom. Overall, sequence of the junctions is largely conserved. Notably, the bases (in a red box) involved in RNA-RNA long-range interactions between H$_4$ and H$_5$ are highly conserved, especially the binding receptor (A$_{234}$, G$_{240}$, and C$_{241}$) of the GNRA loop in H$_4$ which is nearly perfectly conserved.

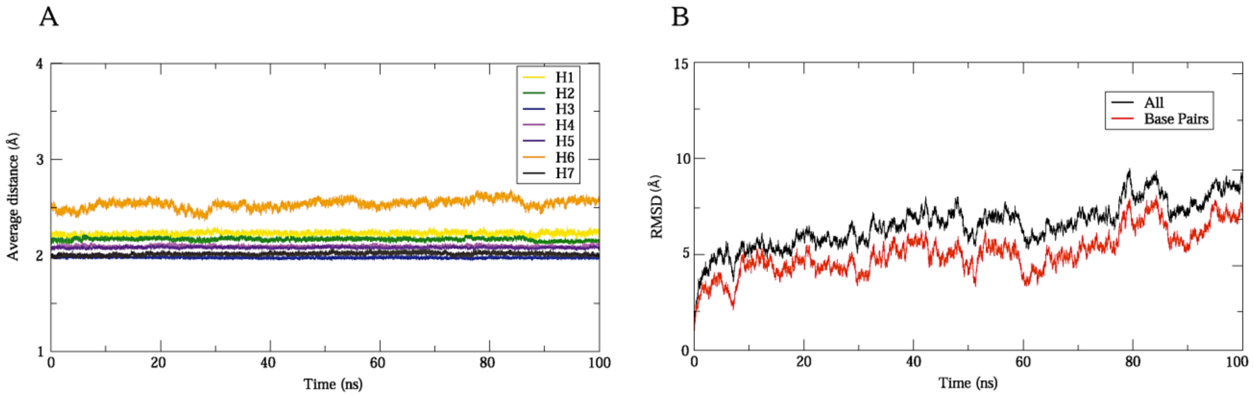

Figure S2. Average distance of base pairs in helices **(A)** and RMSDs of the entire system (116 residues) and only base pairs (82 residues) with respect to the starting structure, respectively **(B)**.

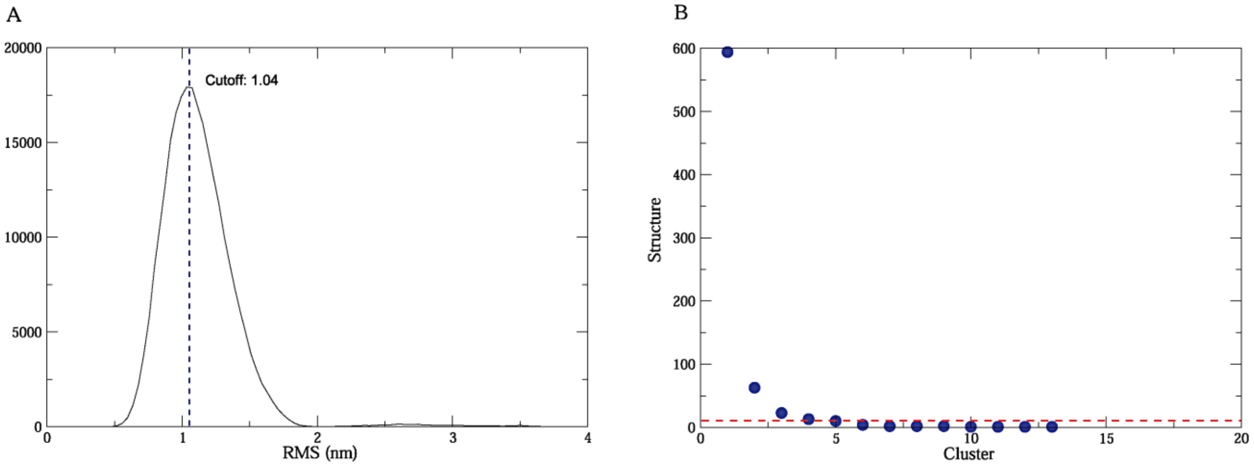

Figure S3. RMSD distribution and clustering analysis of the 717 structures based on the basal region, G_{86} to U_{133} and C_{249} to C_{299}, in domain 3. The 3D models are obtained using 2D information of the basal region in FMDV C-S8 IRES domain 3. With equally distributed 101 bins formed between zero and a maximum RMSD value of 3.97 nm, each RMSD value from either upper or lower triangular RMSD matrix (717 × 717) is put into a right bin. The cutoff value of 1.04 separates the peak **(A)**. Clustering analysis of the 717 structures is based on the overall helical shape of the basal region. The RMSDs of these structures range from 0.44 to 3.97 nm. Thirteen clusters are found, of which the first four clusters contain at least 10 structures **(B)**.

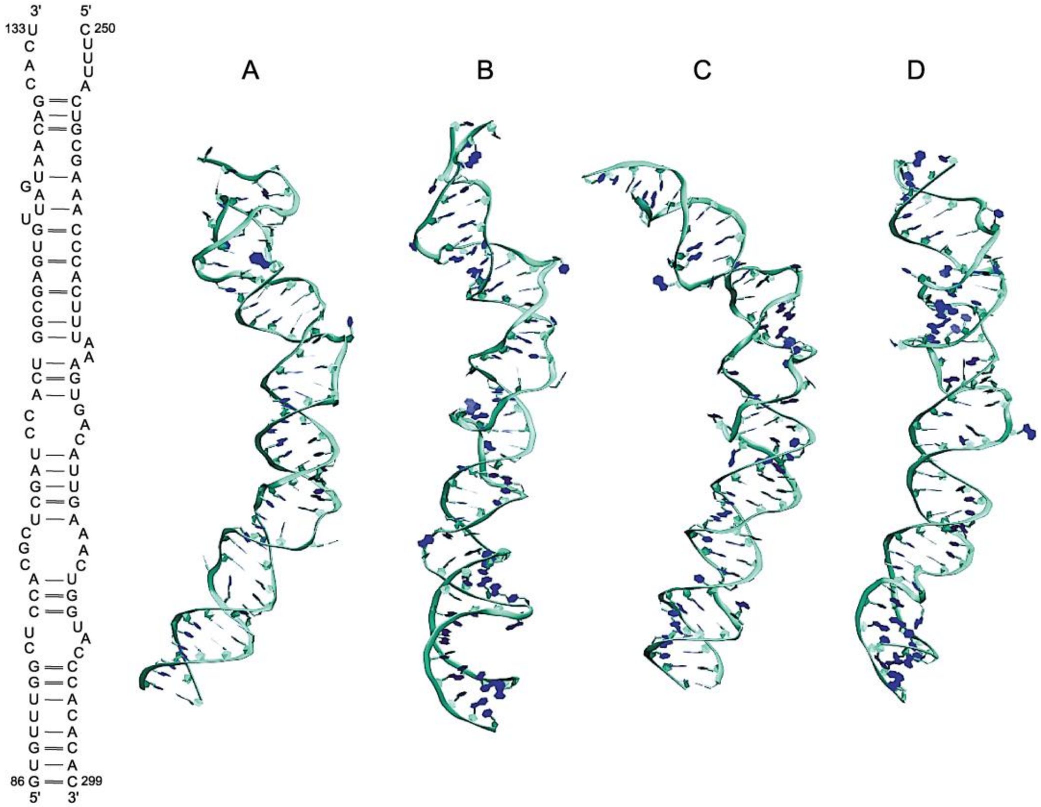

Figure S4. Candidate 3D models of the basal region in FMDV IRES domain 3. These four representative models are selected from the first four large clusters containing **(A)** 594, **(B)** 64, **(C)** 23, and **(D)** 13 structures, respectively (see Fig. S3B). Overall shape and orientation of the helical axis of these four structures are similar with some flexibility (e.g., bending) in unpaired regions.

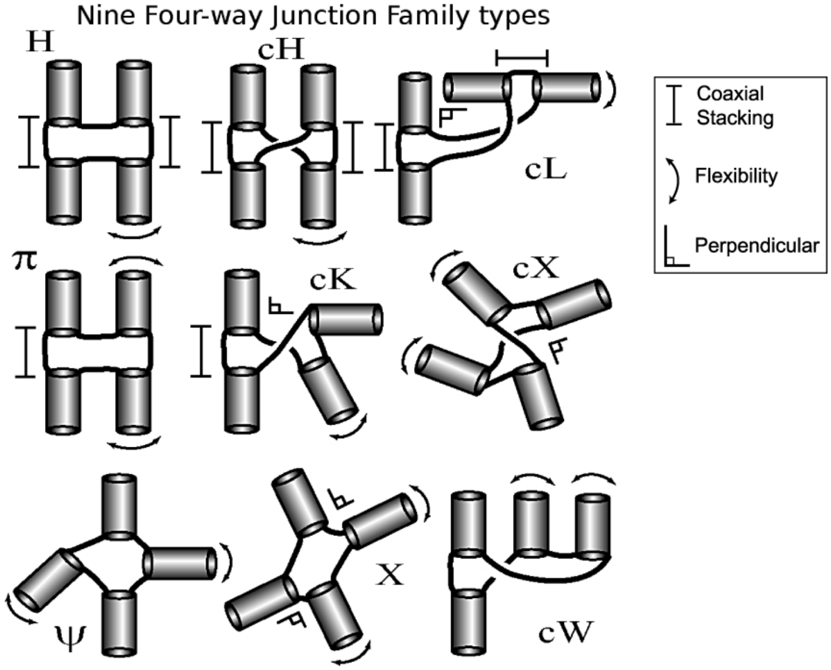

Figure S5. Schematic representation of four-way junction families. There are nine families in four-way junction—*H*, *cH*, *cL*, *cK*, *π*, *cW*, *Ψ*, *cX* and *X*—mainly determined by coaxial stacking and overall helical arrangements. The three family types, *H*, *cH* and *cL*, contain two coaxial stacking patterns; the coaxially stacked helices in *H* and *cH* are parallel to each other while *cL* has a perpendicular arrangement between coaxially stacked helices requiring relatively long single strands. The other six family types contain either one or no coaxial stacking patterns.

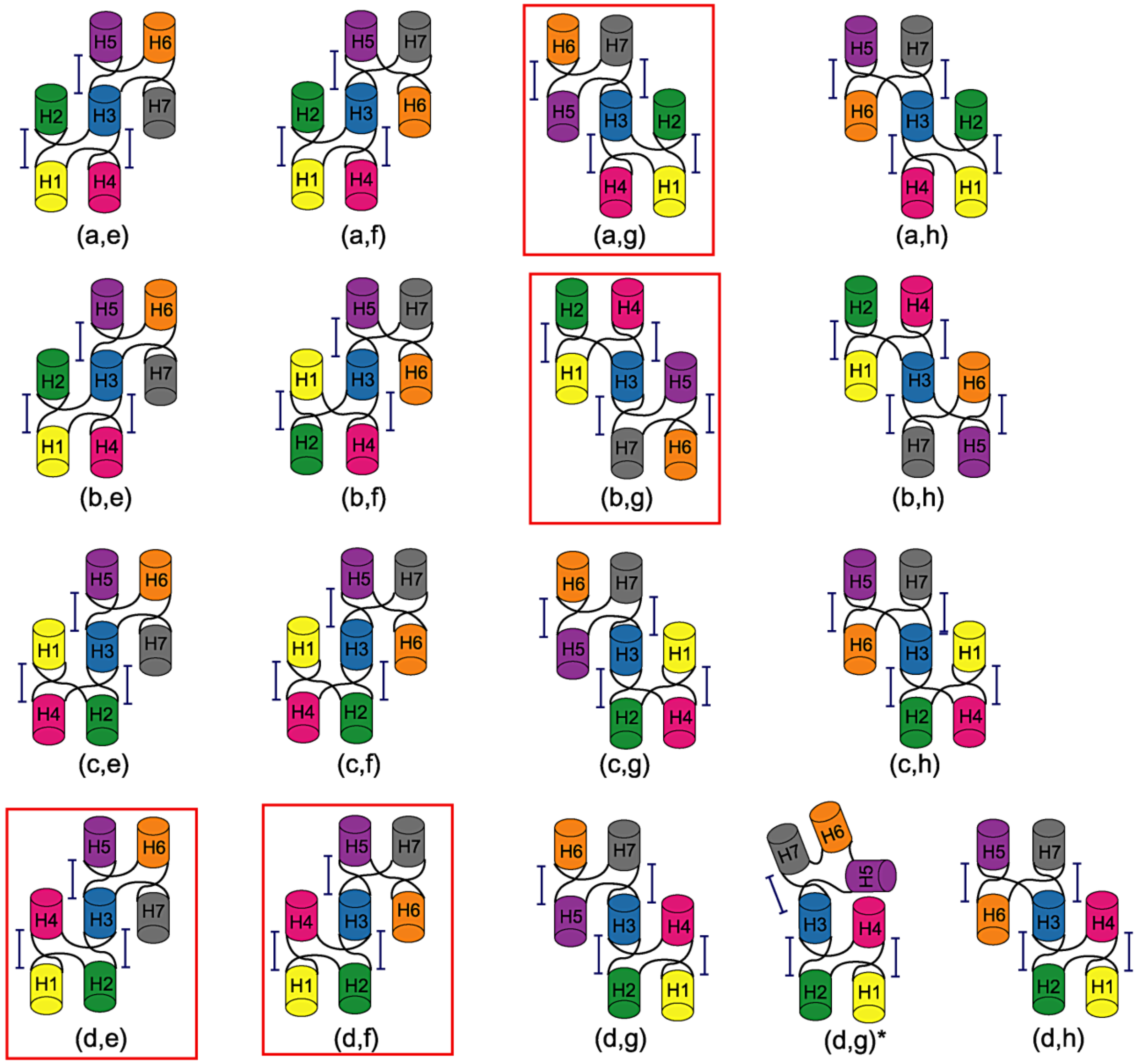

Figure S6. 17 combinations of two four-way junction topologies including (d,g)*, a modified combination of (d,g), with shown in Fig. 4B. The four combinations (a,g), (b,g), (d,e) and (d,f) are highlighted with red box as candidate topologies considering potential long-range interactions between H_4 and H_5.

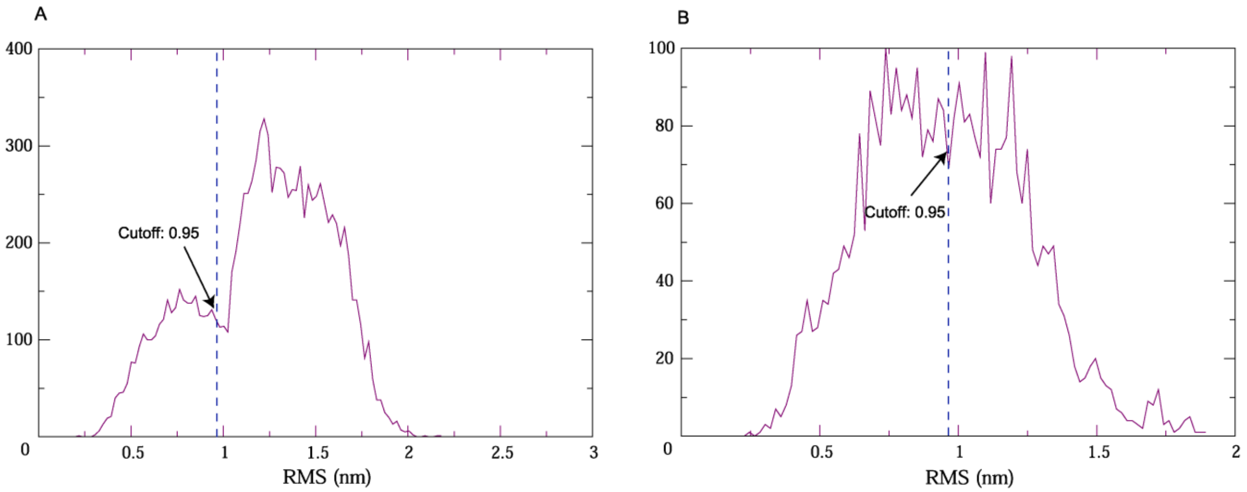

Figure S7. RMSD distribution of two subgroups, 160 ($H_1H_2\_H_3H_4$) and 107 ($H_1H_4\_H_2H_3$) structures respectively, for the 267 structures based on the helical arrangements in Junction I. The 3D models are obtained using a distance constraint between A_{180} and $C_{232}G_{240}$. With equally distributed 101 bins formed between zero and maximum RMSD values ((A) 2.36 and (B) 2.10 nm), each RMSD value from either upper or lower triangular RMSD matrix ((A) 160 × 160 and (B) 107 × 107) is put into a right bin. The cutoff values of 1.0 and 0.96 separate the two peaks in (A) and (B).

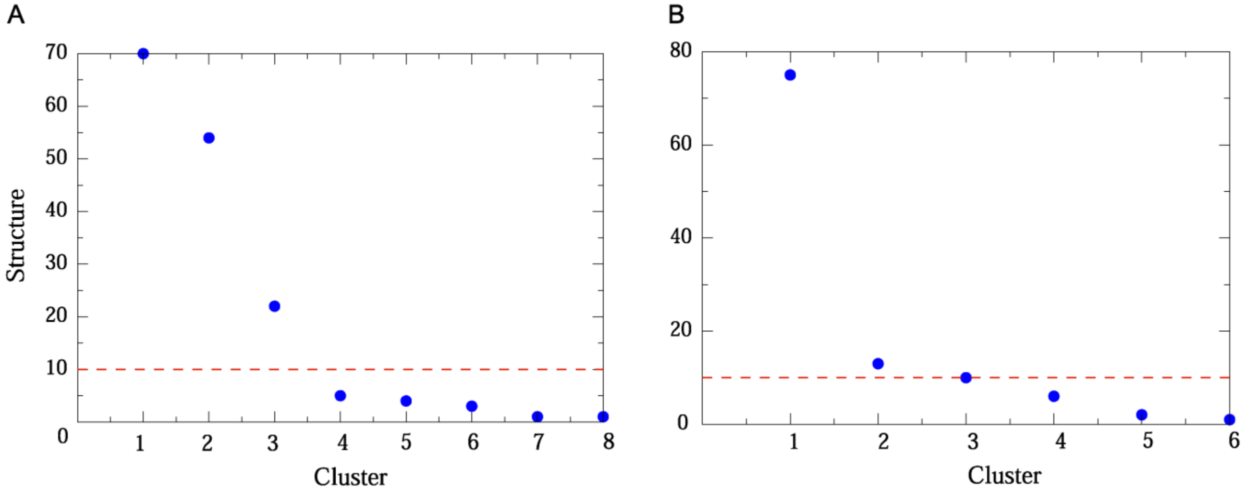

Figure S8. Clustering analysis of the two subgroups, of 160 ($H_1H_2\_H_3H_4$) and 107 ($H_1H_4\_H_2H_3$) structures respectively, in 267 structures based on the helical arrangements in Junction I. The 3D models are obtained using a distance constraint between A_{180} and $C_{232}G_{240}$. The RMSDs of structures in (A) and (B) range from 0.22 to 2.36 nm and from 0.25 to 2.10 nm, respectively. Eight and six clusters are found in (A) and (B), of which the first three clusters for both (A) and (B) contain at least 10 structures.

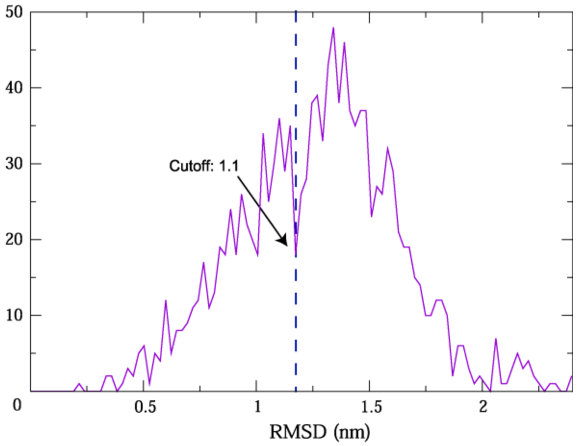

Figure S9. RMSD distribution of 52 structures, 49 ($H_1H_2\_H_3H_4$) and 3 ($H_1H_4\_H_2H_3$). The 3D models are obtained using a distance constraint between A_{180} and $G_{229}C_{243}$. With equally distributed 101 bins formed between zero and the maximum RMSD value of 2.39 nm, each RMSD value from either upper or lower triangular RMSD matrix (52 × 52) is put into a right bin. Although determining cutoff values is not clear cut due to the indefinite two peaks in the distribution and a relatively small number of structures, we find a reasonable cutoff value of 1.1 nm.

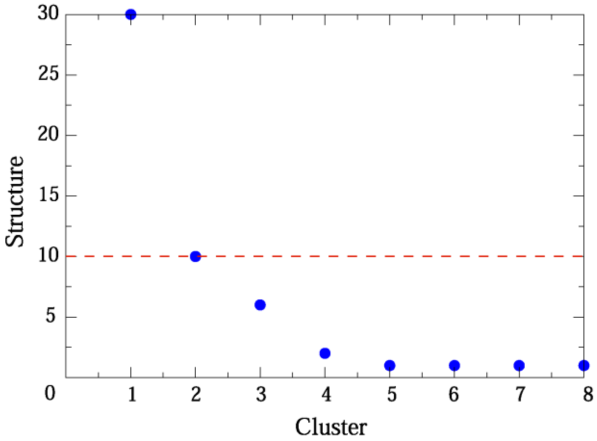

Figure S10. Clustering analysis for the 52 structures, mainly 49 for $H_1H_2\_H_3H_4$ and 3 for $H_1H_4\_H_2H_3$. The 3D models are obtained using a distance constraint between A_{180} and $G_{229}C_{243}$. The RMSDs of structures range from 0.20 to 2.39 nm. The first two of eight clusters contain at least 10 structures.

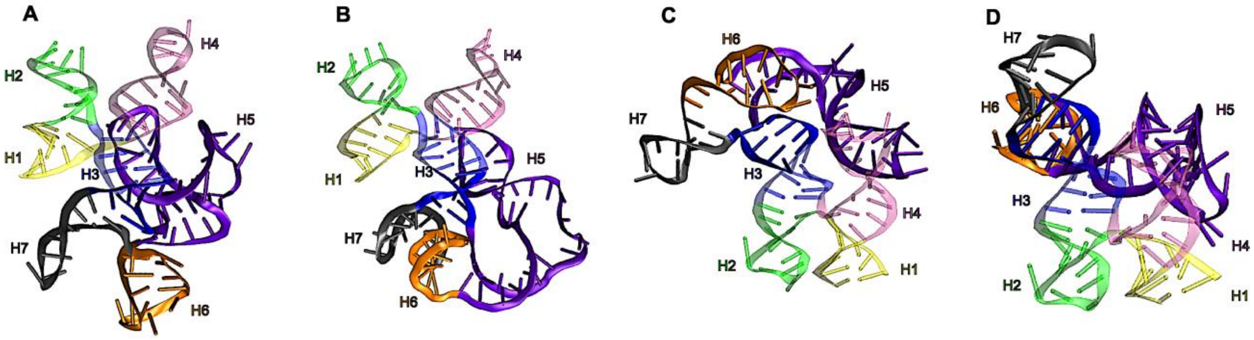

Figure S11. Candidate 3D models of FMDV IRES domain 3 targeting the G_{229}/C_{243} base pair as a receptor of GUAA tetraloop. The structures are unorganized in junction II comparing to the candidate models in Fig. 5. Note that **(A)** and **(B)** are from the two clusters in Fig. S4 while **(C)** and **(D)** are chosen among the three decoys for H_1H_4_H_2H_3.

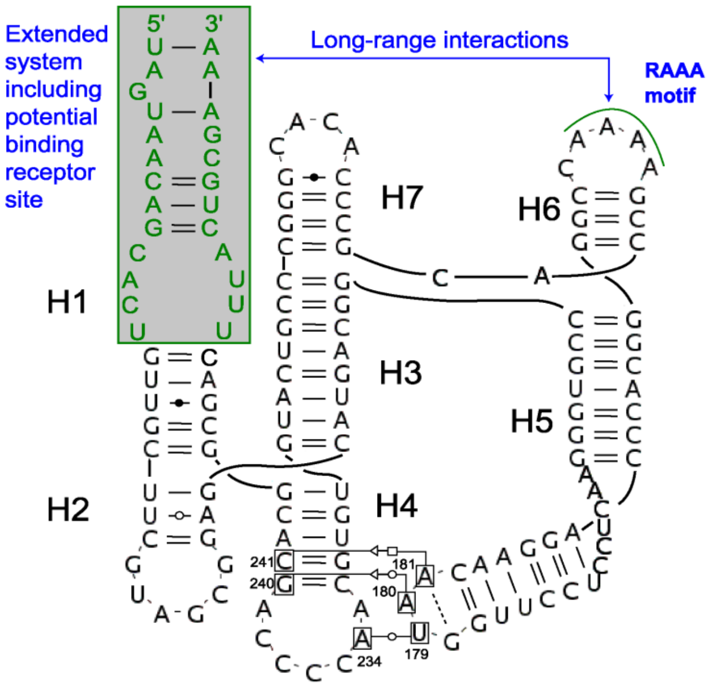

Figure S12. An extended 2D structure of the apical region including a potential binding receptor site of RAAA motif. Experimental data suggests long-range interactions between RAAA motif and the extended system ($U_{121}\ldots A_{261}$). In 3D space, the plane of junction I and II are perpendicular that the spatial distance between these structural elements involving RAAA long-range interactions are relatively close.

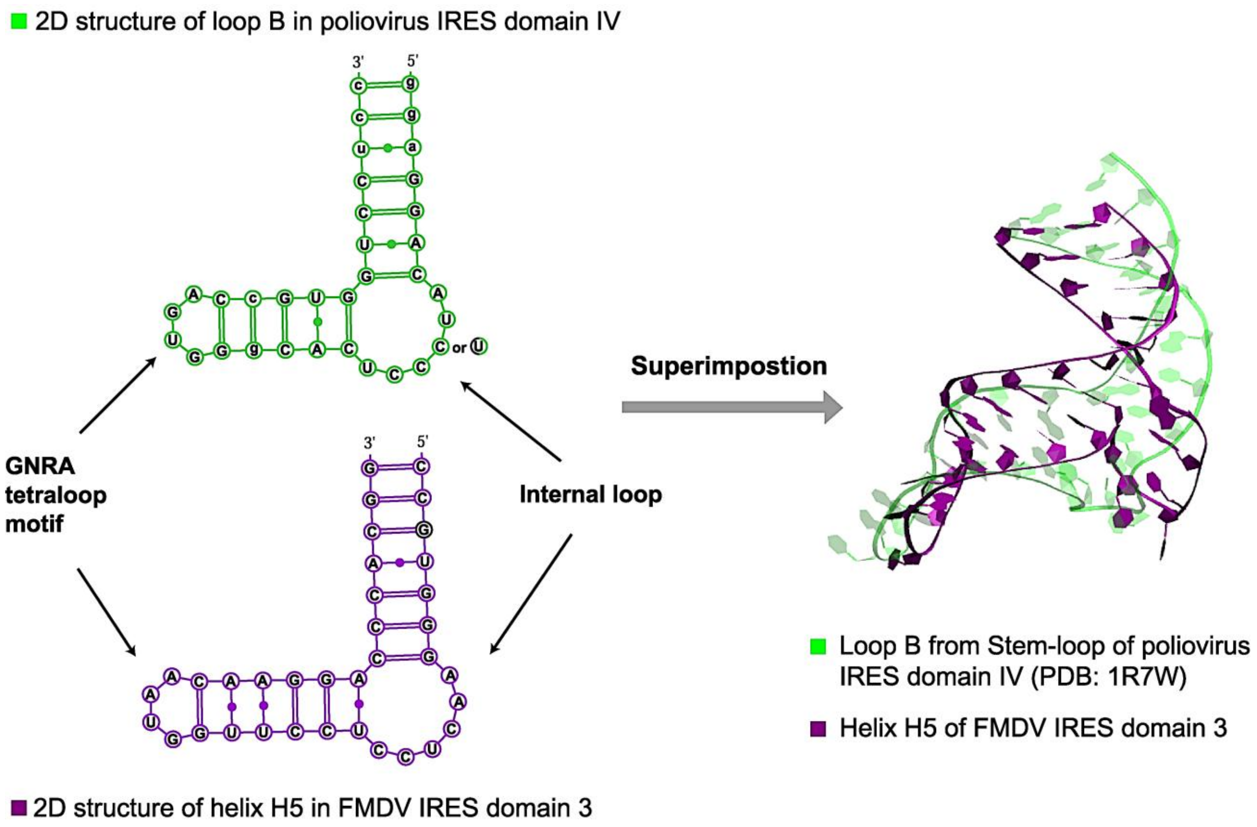

Figure S13. The shape of helix H5 agrees well with an L-shaped native structure of a poliovirus IRES domain IV. In addition, the helix H5 containing GNRA motif is compared to the NMR data of loop B, equivalent in poliovirus IRES containing GNRA motif. Although the sequences are different, overall shapes of both structures agree well with RMSD value of 7.5 Å.

Table S1. Sequences of GNRA loop in 318 FMDV IRES domain 3

Sequence	GUAA	GUGA	GCAA	GCGA	GAGA
Count	233	54	22	8	1

Table S2. List of FMDV IRES sequences.

Seq. no.	Accession no.	Description (type, strain or isolate)
1	FJ824812	C strain C-S8p200
2	DQ409190	C isolate C-S8p460d951
3	AM409325	C isolate H595
4	AY593805	C isolate c1ober iso88
5	AY593804	C isolate c1noville iso56
6	AJ133358	C isolate rp99
7	AJ133359	C isolate rp146
8	AY593808	C4 isolate C4 Tierra del Fuego iso2
9	AY593806	C3 isolate c3ind iso19
10	AY593757	A isolate a17 Aguarulbos iso83
11	AY593803	A isolate avenceslau iso70
12	AY593753	A isolate a13brazil iso75
13	AY593787	A isolate abage iso63
14	AY593758	A isolate a18zulia iso40
15	AY593788	A isolate abrazil iso67
16	AY593756	A isolate a16belem iso80
17	AY593781	A isolate a5westerwald iso73
18	AY593778	A isolate a4spain iso62
19	AY593754	A isolate a14 spain iso39
20	AY593752	A isolate a12valle 119 iso20
21	M32257	A-12
22	AY593821	O isolate o1caseros iso35
23	AY593792	A isolate aparma iso55
24	AY593780	A isolate a5allier iso45
25	AY593789	A isolate acanefa iso48
26	AY593769	A isolate a25 argentina iso38
27	AY593771	A isolate a27columbia iso78
28	AY593760	A isolate a20ussr iso10
29	AY593826	O isolate o2brescia iso17
30	AY593807	C3 isolate c3resende iso1
31	M10975	A12 strain 119
32	AY593779	A isolate a4wg iso72
33	AY593777	A isolate a4 W Germany iso42
34	AY593794	A isolate asabana iso68
35	AY593767	A isolate a24 argentina iso9
36	D10146	C3R-O/E
37	AY593774	A isolate a2spain iso7
38	AY593768	A isolate a24cruzeiro iso71
39	AY593796	Asia 1 isolate asia1-2isrl3-63 iso6
40	AY593827	O isolate o3venezuela iso15
41	AY593822	O isolate o1m11 iso57
42	HQ009509	O strain China/5/99(Fujian)
43	AY593810	C isolate cwald iso32
44	AY593809	C5 isolate c5arg iso60
45	AY593775	A isolate a32ven iso36
46	AY593773	A isolate a29peru iso37
47	HQ832585	A isolate IND 26/2006
48	DQ533483	Asia 1 strain ZB/CHA/58(att)
49	AY593795	Asia 1 isolate asia1-1pak iso3
50	HQ832580	A isolate IND 818/2003
51	AY593764	A isolate a22iraq70 iso92
52	AY593763	A isolate a22iraq64 iso86
53	AY593762	A isolate a22iraq-95 iso95
54	X74812	A strain A22/550 Azerbaijan 65
55	AY593829	O isolate o6pirbright iso58
56	AY593819	O isolate o1Campos94 iso94
57	AY593818	O isolate o1Campos iso96
160	AY304994	Asia 1 IND 63/72
161	AY593755	A isolate a15thailand iso43
162	AJ633821	O isolate FRA/1/2001
163	AJ539141	O strain UKG/35/2001
164	AJ539137	O strain TAW/2/99 BOV
165	Y17973	Asia isolate Asia 1 63/72
166	AB079061	O strain O/JPN/2000
167	DQ989321	Asia 1 isolate IND 438-01
168	DQ989320	Asia 1 isolate IND 182-02
169	DQ404160	O strain UKG/14524/2001
170	DQ404159	O strain UKG/14603/2001
171	DQ404158	O strain UKG/15101/2001
172	AY593793	A isolate aphilippines iso50
173	JN099702	A isolate 4258 strain A/IRQ/09
174	JN099701	A isolate 4257 strain A/IRQ/09
175	JN099690	A isolate 4236 strain A/IRQ/09
176	FJ175666	O isolate Israel 07-6387
177	FJ175662	O isolate Israel 07-6380
178	FJ175661	O isolate Israel 07-6378
179	EF494487	A isolate PAK1
180	EF117837	A isolate Lindholm 1.3 PAK3/2006
181	HQ832581	A isolate IND 64/2004
182	EF552697	O/UKG/5681/2001
183	EF552694	O/UKG/4998/2001
184	EF552692	O/UKG/7299/2001
185	DQ989316	Asia 1 isolate IND 21-89
186	DQ989313	Asia 1 isolate IND 52-87
187	DQ989309	Asia 1 isolate IND 82-96
188	DQ989308	Asia 1 isolate IND 397-97
189	DQ404163	O strain UKG/14339/2001
190	DQ404162	O strain UKG/14476/2001
191	DQ404161	O strain UKG/14391/2001
192	AY312587	O strain PanAsia isolate O/SKR/2000
193	AY593824	O strain O1SKR isolate o1skr iso85
194	AJ539140	O strain SAR/19/2000
195	AJ539139	O strain SKR/2000
196	HQ832586	A isolate IND 43/2006
197	HQ832579	A isolate IND 281/2003
198	HM854024	A strain IND17/82
199	DQ989317	Asia 1 isolate IND 148-01
200	DQ989314	Asia 1 isolate IND 354-01
201	JN099703	A isolate 4253
202	JN099700	A isolate 4256
203	JN099699	A isolate 4255
204	JN099697	A isolate 4252
205	JN099694	A isolate 4240
206	JN099692	A isolate 4238
207	JN006722	A isolate A/SIN/PAK/L4/2008
208	HQ632770	O isolate MAY/1/2004
209	FJ593963	A isolate IND83/97
210	EF494488	A isolate PAK5/2006
211	EF494486	A isolate AIRN2005_WRL
212	AY593797	Asia 1 isolate asia1-3kimron iso61
213	AY593766	A isolate a23kenya iso8
214	HQ832582	A isolate IND 249/2004
215	FJ542367	O isolate UKG/1558/2001
216	AF377945	O/SKR/2000

58	AJ320488	O isolate o1Campos/Bra/58	217	DQ989319	Asia 1 isolate IND 423-01
59	M95781	C isolate Campos (stock 507)	218	AY593813	O isolate o11indonesia iso52
60	HM008917	O strain O/YS/CHA/05	219	JN006721	Asia 1 isolate As/SIN/PAK/L2812/2009
61	DQ989311	Asia 1 isolate IND 37-02	220	JN006720	Asia 1 isolate As/SIN/PAK/L2810/2009
62	AY593751	A isolate a10holland iso82	221	HQ832584	A isolate IND 22/2006
63	AJ007347	Isolate C3Arg85	222	HQ832578	A isolate IND 161/2003
64	FJ593975	A isolate IND461/02	223	HM854021	A strain IND81/00
65	FJ593964	A isolate IND100/06	224	GQ406247	A strain A/VN/09/2009
66	AY333431	O isolate O/NY00	225	AY593812	O isolate o10phil76 iso76
67	AY593790	A isolate a general lopez iso102	226	AY593811	O isolate o10phil54 iso54
68	AY593765	A isolate a22turkey iso66	227	HQ832583	A isolate IND 447/2005
69	M32258	A-10	228	HQ113232	O isolate O/ISL/PAK/L1573/2009
70	EU448373	O isolate UKG/93/2007 (IP2b)	229	AY312589	O isolate O/SKR/2002
71	EU448372	O isolate UKG/7B/2007 (IP1b)	230	AY593772	A isolate a28 Turkey iso44
72	EU448371	O isolate UKG/7/2007 (IP1b)	231	Y17974	O Bak/90
73	EU448370	O isolate O1/BFS 1860/UK/67 (MAH)	232	JF739177	Asia 1 isolate As1/Shamir/89
74	EU448369	O isolate O1/BFS 1860/UK/67 (IAH2)	233	HQ832592	A isolate IND 17/2009
75	EU448368	O isolate O1/BFS 1860/UK/67 (IAH1)	234	DQ989323	Asia 1 isolate IND 97-03
76	AY593830	O isolate o7poland iso49	235	DQ989322	Asia 1 isolate IND 139-02
77	AY593820	O isolate o1canefa iso59	236	AY593800	Asia 1 isolate asia1leb83 iso28
78	AY593817	O isolate o1brugge iso79	237	AY593799	Asia 1 isolate asia1leb4 iso4
79	AY593816	O isolate o1bfs46 iso46	238	AY593798	Asia 1 isolate asia1leb-89 iso89
80	AY593815	O isolate o1bfs iso18	239	HM854025	A strain IND40/00
81	AY593770	A isolate a26arg iso74	240	GQ406248	A strain A/VN/02/2009
82	D10144	Strain O1C-O/E	241	AY593828	O isolate o5india iso34
83	HQ832576	A isolate IND 21/1990	242	JQ900581	O strain O/GSLX/2010
84	AY593823	O isolate o1manisa iso87	243	JN998085	O strain O/BY/CHA/2010
85	AY593814	O isolate o1argentina iso5	244	HQ632768	O isolate MAY/3/2000
86	AY593786	A isolate aarg Trenquelauquen iso103	245	FJ593969	A isolate IND241/04
87	AY593785	A isolate aargp64 iso100	246	DQ989315	Asia 1 isolate IND 47-93
88	AY593784	A isolate aargp55 iso99	247	DQ989318	Asia 1 isolate IND 61-02
89	AY593783	A isolate aarg2001 iso93	248	DQ989305	Asia 1 isolate IND 116-90
90	HQ832588	A isolate IND 88/2006	249	HQ632773	A isolate MAY/3/2007
91	HQ113233	Asia 1 isolate BAM/AFG/L-590/2009	250	GQ406252	A strain A/VN/20/2009
92	FJ593970	A isolate IND270/03	251	GQ406249	A strain A/VN/03/2009
93	FJ593968	A isolate IND154/03	252	HM229661	O isolate HKN/20/2010
94	FJ593967	A isolate IND153/03	253	HM625674	O isolate O/K/52/1992
95	FJ593962	A isolate IND24/03	254	GU125646	Asia 1 isolate Asia1/VN/LC04/2005
96	EU140964	O strain UAE 7/99	255	FJ593965	A isolate IND104/00
97	DQ989304	Asia 1 isolate IND 334-00	256	EF614457	O strain O/SKR/14/02
98	DQ989303	Asia 1 isolate IND 151-94	257	DQ989312	Asia 1 isolate IND 13-91
99	DQ404164	O strain UKG/11676/2001	258	AY687334	Asia 1 strain IND 491/97
100	AY593837	O isolate ouruguay-51 iso51	259	FJ593974	A isolate IND456/98
101	AY593836	O isolate ouk2001x iso84	260	FJ593972	A isolate IND288/07
102	AY593832	O isolate O UK2001-FB	261	FJ461344	O isolate Kumi District
103	AY593831	O isolate O UK2001-ED	262	HQ268509	A isolate VIT_4/2004
104	AY593825	O isolate o1valle iso64	263	GQ406251	A strain A/VN/16/2009
105	AY593776	A isolate a3mecklenburg iso81	264	AY593782	A isolate a argentina 2000 iso104
106	AY593759	A isolate a1bayern iso41	265	JQ973889	O strain O/CHN/Mya98/33-P
107	AJ539138	O strain Tibet/CHA/99	266	HQ632774	Asia 1 isolate MAY/9/99
108	AJ539136	O strain TAW/2/99 TC	267	AY593834	O isolate orey-iran iso53
109	AF506822	O strain China/1/99(Tibet)	268	HQ832590	A isolate IND 245/2007
110	EU448381	O isolate UKG/2366/2007 (IP8)	269	GU931682	Asia 1 isolate Asia1/YS/CHA/05
111	EU448380	O isolate UKG/1679/2007 (IP7)	270	HM625676	O isolate O/K/117/1999
112	EU448379	O isolate UKG/1484/2007 (IP6b)	271	FJ461345	O isolate Kapchorwa District
113	EU448377	O isolate UKG/800/2007 (IP4b)	272	DQ989307	Asia 1 isolate IND 247-92
114	EU448376	O isolate UKG/1153/2007 (IP3c)	273	AY359854	O strain OMIII
115	EU448375	O isolate UKG/643/2007 (IP3b)	274	DQ119643	O strain HLJOC12/03
116	EU448374	O isolate UKG/150/2007 (IP2c)	275	JN998086	O strain O/GZ/CHA/2010
117	X00871	Strain O1K	276	AY593835	O isolate otaiwan97 iso106/112
118	D10143	strain O1C	277	AY593833	O isolate openghu iso108
119	HQ268524	O isolate BHU_27/2004	278	AF308157	O1 Yunlin Taiwan
120	JN099698	A isolate 4254 strain A/IRQ/09	279	HM854023	A strain IND258/99
121	JN099696	A isolate 4247 strain A/IRQ/09	280	FJ593966	A isolate IND138/99

122	JN099695	A isolate 4244 strain A/IRQ/09	281	EF614458	Asia 1 strain Asia1/MOG/05
123	JN099693	A isolate 4239 strain A/IRQ/09	282	EF149009	Asia 1 strain Jiangsu/China/2005
124	JN099691	A isolate 4237 strain A/IRQ/09	283	HQ832589	A isolate IND 109/2006
125	JN099689	A isolate 4234 strain A/IRQ/09	284	GQ406250	A strain A/VN/11/2009
126	JN099688	A isolate 4235 strain A/IRQ/09	285	FJ593973	A isolate IND360/07
127	JN006719	Asia 1 isolate As/SIN/PAK/L5/2008	286	HM854022	A strain IND17/77
128	FJ175665	O isolate Israel 07-6391	287	HM055510	O isolate O/VN/LC169/2009
129	FJ175664	O isolate Israel 07-6389	288	AF154271	Strain Tau-YuanTW97 isolate Taiwan
130	FJ175663	O isolate Israel 07-6382	289	HQ631363	Asia 1 isolate Asia1/1/YZ/CHA/06
131	FN594747	Strain O1 Manisa	290	AF026168	O strain Chu-Pei complete genome
132	FJ593971	A isolate IND287/96	291	HM625675	O isolate O/K/109/2000
133	DQ989310	Asia 1 isolate IND 101-99	292	AY317098	Strain HKN/2002
134	AY390432	Asia1 strain YNBS/58	293	HQ832591	A isolate IND 437/2008
135	AY593802	A isolate A uruguay 2001 iso98	294	FJ906802	Asia 1 strain Asia1/WHN/CHA/06
136	AY593801	A isolate A30 Uruguay/68 iso90	295	GU125649	O isolate O/VN/SL21/2006
137	AY687333	Asia 1 isolate IND 321/01	296	GU125648	O isolate O/VN/SL01/2006
138	HQ632769	O isolate MAY/7/2001	297	GU125647	O isolate O/VN/SL22/2006
139	GU384683	O isolate PAK/45/2008	298	HQ832587	A isolate IND 50/2006
140	GU384682	O isolate PAK/44/2008	299	HM625677	O isolate O/U/25/2006
141	EU214601	O strain UKG/8098/2001	300	HQ832577	A isolate IND 110/1999
142	EF552696	O/UKG/5470/2001	301	HM191257	O isolate O/U/312/2006
143	EF552695	O/UKG/9443/2001	302	AY593791	A isolate airan iso105
144	EF552693	O/UKG/4014/2001	303	GU125645	Asia 1 isolate Asia1/VN/QT03/2007
145	EF552691	O/UKG/9161/2001	304	HM625673	O isolate O/K/48/2005
146	EF552690	O/UKG/7039/2001	305	HQ412603	O strain O/YM/YN/2000
147	EF552689	O/UKG/4141/2001	306	EF149010	Asia 1 strain Asia 1/HNK/CHA/05
148	EF552688	O/UKG/3952/2001	307	EF175732	O isolate WFL
149	DQ989306	Asia 1 isolate IND 81-86	308	EF611987	O isolate O/Uganda/2006
150	DQ404175	O strain UKG/173/2001	309	HQ632772	O isolate MAY/7/2007
151	DQ404173	O strain UKG/220/2001	310	HQ632771	O isolate MAY/8/2005
152	DQ404172	O strain UKG/621/2001	311	AY686687	O isolate ES/2001
153	DQ404171	O strain UKG/4569/2001	312	DQ248888	O isolate lz
154	DQ404169	O strain UKG/7038/2001	313	AY593761	A isolate a21kenya iso77
155	DQ404170	O strain UKG/7675/2001	314	AF511039	O strain Akesu/58
156	DQ404168	O strain UKG/9011/2001	315	DQ478936	O strain OGBF15
157	DQ404167	O strain UKG/9327/2001	316	DQ478937	O strain OGBF15 derivative
158	DQ404166	O strain UKG/9788/2001	317	AY593844	SAT 1 isolate sat1-7isrl iso12
159	DQ404165	O strain UKG/9964/2001	318	FJ461346	SAT 2

Table S3. Alignment of 318 FMDV IRES sequences. Sequence number (Seq. no.) is shown in the first column followed by aligned sequences. The apical region of domain 3 is marked in a shaded background.

Seq. no.	Aligned sequences
310	AGCAGGTTTCCGCAACT-GATAAAAAC-CCGTGCATTTTGGAACCCCGCCTGGTCTTTCC
311	AGCAAGTTTCCACAACT-GA-GAAAAC-TCGTGCAACTTGGAACCCCGCCTGGTCTTTCC
307	AGCAGGTTTCCACAACT-GATA-AAAC-TCGTGCATTTTGAAGCCCCGCCTGGTCCTTCC
308	-GCAGGTATCCACAACT-GACACAAAA-CCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
306	--CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
276	AGCAGGTTTCCACAACT-GATAAAAC--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
277	AGCAGGTTTCCACAACT-GATAAAAC--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
278	AGCAGGTTTCCACAACT-GATAAAAC--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
288	AGCAGGTTTCCACAACT-GATAAAAC--TCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
305	AGCAGGTTTCCACAACT-GATAAAAC--CCGTGCATTTTGAAACCCCGCCTGGTCTTTCC
290	AGCAGGTTTCCACAACT-GATAAAAC--TCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
292	AGCAGGTTTCCACAACT-GATAAAAC--TCGTGCATTTTGAAACCCCGCCTGGTCTTTCC
244	--CAGGTTCCCACAACC-GACACA-AA-CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
257	AGCAGGTTCCCACAACT-GACACA-AA-CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
299	-GCAGGTATCCACAACT-GACACAGAA-CCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
245	-GCAGGTCTCCACAACT-GATACAAA--TCGTGCAACTTGAAACCCCGCCTGGTCTGTCC
258	---AGGTTTCCACAACT-GACACAAA--CCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
236	-GCAGGTCTCCACAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
246	-GCAGGTTTCCACAACT-GACACACA--ACGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
259	-GCAGGTTTCCACAACT-GACACACA--TCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC

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268          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
280          -GCAGGTTTCCACAACT-GACACACA--TCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
247          -GCAGGTTTCCACAACT-GACACAGA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
220          -GCAGGTTTCCACAACT-GACACACA--TCGTGCAATTTGAAACCCCGCCTGGTCTTTCC
222          -GCAGGTCTCCACAACT-GACACAGA--TCGTGCAACCTGAAACTCCGCCTGGTCTTTCC
238          -GCAGGTCTCCACAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
248          -GCAGGTTTCCACAACT-GACACGAA--CCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
261          -GCAGGTATCCACAACT-GACACAAAA-CCGTGCAATTTGAAGCTCCGCCTGGTCTTTCC
249          -GCAGGTCTCCACAACT-GACACAAA--ACGTGCAACTTGAAACCCCGCCTGGTCTTTCC
293          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
294          -GCAGGTTTCC-CAACC-GACACAAC--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
295          -GCAGGTTCCCACAACC-GACACAAA--CCGTGCAATTTGAAATCCCGCCTGGTCTTTCC
296          -GCAGGTTCCCACAACC-GACACAAA--CCGTGCAATTTGAAATCCCGCCTGGTCTTTCC
260          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
61           AGCAGGTCTCCACAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTAGTTTTTCC
132          -GCAGGTTTCCACAACT-GACACACA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
125          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
126          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
173          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
204          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
174          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
175          -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
205          -GCAGGCTTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
127          -GCAGGTTTCCACAACT-GACACACACACCGTGCAATCTGAAACTCCGCCTGGTCTTTCC
218          --CAGGTTTCCTCAACT-GACACAAA--CCGTGCAATCTGCAGCTCCGCCTGGTCTTTCC
217          -GCAGGTTTCCACAACT-GACACACA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
133          -GCAGGTTTCCACAACT-GACACACA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
225          -GCAGGTCTCCACAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
228          -GCAGGTTTCCACAACT-GACACACA--CCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
255          -GCAGGTTTCCACAACT-GACACACA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
266          -GCAGGTTCCCACAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
1            AGCAGGTTTCCCCAACT-GACACAAA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
2            AGCAGGTTTCCCCAACT-GACACAAA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
3            AGCAGGTTTCCCCAACT-GACACAAA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
4            AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
5            AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
7            AGCAGGTTTCTCCAACT-GACACAAA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
9            -GCAGGTTTCCCCAACT-GACACAAC--CCGTGCAACTTGAAACTCCGCTTGGTCTTTCC
6            AGCAGGTTTCTCCAACT-GACACAAA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
8            -GCAGGTTTCCCCAACT-GACACACA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
10           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
12           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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23           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCATTCC
18           AGCAGGTTTCTCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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14           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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24           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
35           --CAGGCTCCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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36           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
15           -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAGCTTGGCGCTCCGCCTGGTCTTTCC
21           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAATTTGGAACTCCGCCTGGTCTTTCC
20           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAATTTGGAACTCCGCCTGGTCTTTCC
27           AGCAGGTTTCTCCAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGTCTTTCC
16           -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
17           AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
79           -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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26               AGCAGGTCCCCCCAACT-GACACAAA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
38               AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAATTTGAAACTCCGCCTGGGCTTTCC
28               AGCAGACTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
34               -GCAGGTTTCCCCAACT-GACACACA--CCGTGCAAATTGAAACTCCGCCTGGTCTTTCC
29               -GCAGGTTTCCCCAACT-GACACTAA--CCGTGCAACTTGAAATCCCGCCTGGTCTTTCC
39               -GCAGGTTTCCCCAACT-GACACAAA--ACGTGCAACTTGAAACCCCGCCTGGTCTTTCC
40               -GCAGGTTTCCCCAACT-GACACTAA--CCGTGCAACTTGAAATCCCGCCTGGTCTTTCC
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84               -GCAGGTTTCCACAACT-GACACAAA--CCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
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53               -GCAGGTTTCCACAACT-GACACGAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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41               -GCAGGTTTCCCCAACT-GACACTAA--CCGTGCAACTTGAAATCCCGCCTGGTCTTTCC
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98               -GCAGGTAGCCCCAACT-GACACAAA--CCGTGCAACTTGGAACCCCGCCTGGTCTTTCC
44               AGCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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56               -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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69               -GCAGGTTTCCCCAACT-GACACTTA--CCGTGCAACTTGAAATCCCGCCTGGTCTTTCC
70               -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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166              --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
215              --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
103              --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
42               --CAGGTTTCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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45      -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
62      -GCAGGTTTCCCCAACT-GACACTTA--CCGTGCAACTTGAAATCCCGCCTGGTCTTTCC
86      -GCAGGTTTCCCCAACC-GACACAAA--CCGTGCAATCTGAAGTTCCGCCTGGTCTTTCC
88      -GCAGGTTTCCCCAACC-GACACAAA--CCGTGCAATCTGAAGTTCCGCCTGGTCTTTCC
87      -GCAGGTTTCCCCAACC-GACACAAA--CCGTGCAATCTGAAGTTCCGCCTGGTCTTTCC
135     -GCAGGTTTCCCCAACC-GACACAAA--CCGTGCAATCTGAAGTTCCGCCTGGTCTTTCC
85      -GCAGGTTTCCCCAACT-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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199     -GCAGGTTTCCACAACT-GACACACA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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207     -GCAGGTTTCCACAACT-GATACACA--TCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
219     -GCAGGTTTCCACAACT-GACACACA--TCGTGCAATTTGAAACCCCGCCTGGTCTTTCC
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177     -GCAGGTTTCCACAACT-GACACACA--TCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
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89      -GCAGGTTTCCCCAACC-GACACAAA--CCGTGCAATCTGAAGTTCCGCCTGGTCTTTCC
95      -GCAGGTCTCCACAACT-GACACAAA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
158     --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
211     -GCAGGATTCCACAACT-GACACAAA--CCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
147     --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
163     --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
96      --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACCTGAAACTCCGCCTGGTCTTTCC
159     --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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176     -GCAGGTTTCCACAACT-GACACACA--TCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
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185     -GCAGGTTCCCACAACT-GACACAAA--CCGTGCAGTTTGAAACTCCGCCTGGTCTTTCC
97      -GCAGGTAGCCCCAACT-GACACAAA--CCGTGCAACTTGAAACCCCGCCTGGTCTTTCC
164     --CAGGTACCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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243     --CAGGTTCCCACAACC-GACACAAA--ACGTGCAACTTGAAATCCCGCCTGGTCTTTCC
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265                 -------TCCCGCAACC-GACACAAA--ACGTGCAACTTGAAATCCCGCCTGGTCTTTCC
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93                  -GCAGGTCTCCACAACT-GACACAAA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
94                  -GCAGGTCTCCACAACT-GACACAAA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
92                  -GCAGGTCTCCACAACT-GACACAAA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
167                 -GCAGGTTTCCACAACT-GACACACA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
168                 -GCAGGTTTCCACAACT-GACACACA--ACGTGCAACTTGAAACTCCGCCTGGTCTTTCC
64                  -GCAGGTCTCCACAACT-GACACAAA--TCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
181                 -GCAGGTCTCCACGACT-GACATAAA--TCGTGCAACTTGAAGCTCCGCCTGGTCTTTCC
141                 --CAGGTTCCCACAACC-GACACAAA--CCGTGCAACTTGAAACTCCGCCTGGTCTTTCC
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2                   TGAATAGGTGACCGGAGGCCGGCACCTTTCC-TTTATAATTAATGACCCT
3                   TGAATAGGTGACCGGAGGCCGGCACCTTTCC-TTTACAATTAATGACCCT
4                   TGAATAGGTGACCGGAGGCCGGCACCTTTTC-TTTA--------------
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23                  TGAATAGGTGACCGGAGGCCGGCACCTTTTC-TTTACA------------
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14                  TGAATAGGTGACCGGAGGCCGGCACCTTTCCTTTTACAA-----------
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15                  TGAATAGGTGACCGGAGGCCGGCACCTTTTC-TTTA--------------
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20                  TGAATAGGTGACCGGAGGCCGGCACCTTT---------------------
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