

Supplementary Figures and Tables

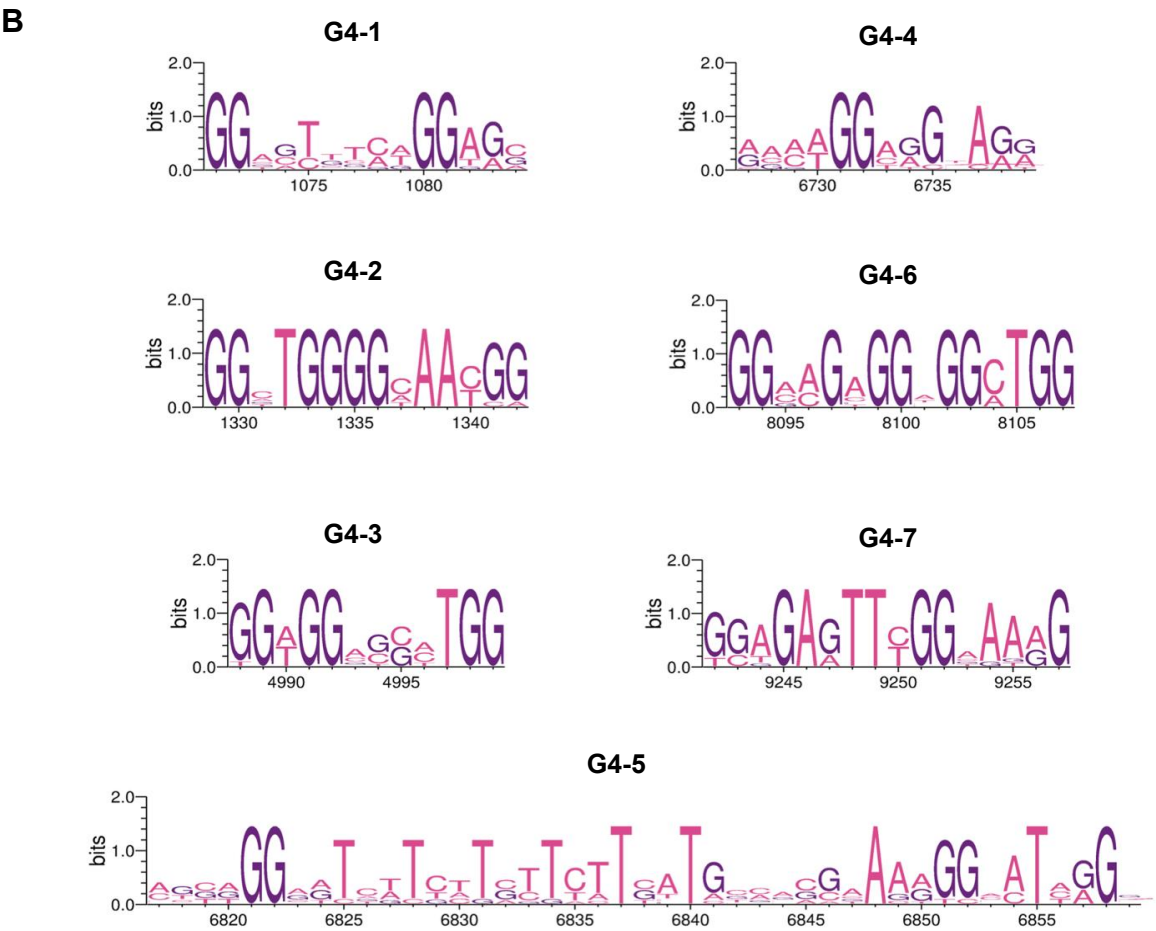
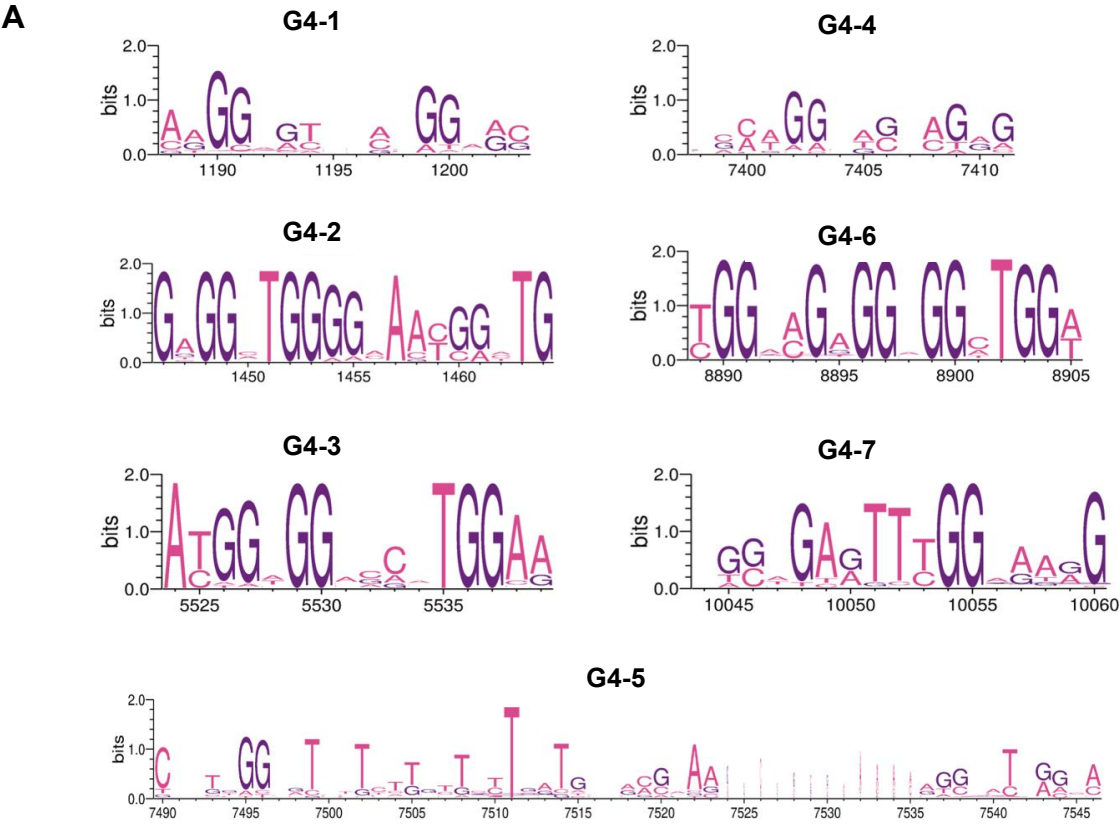


Figure S2. Conservation of G4 motifs across flaviviruses

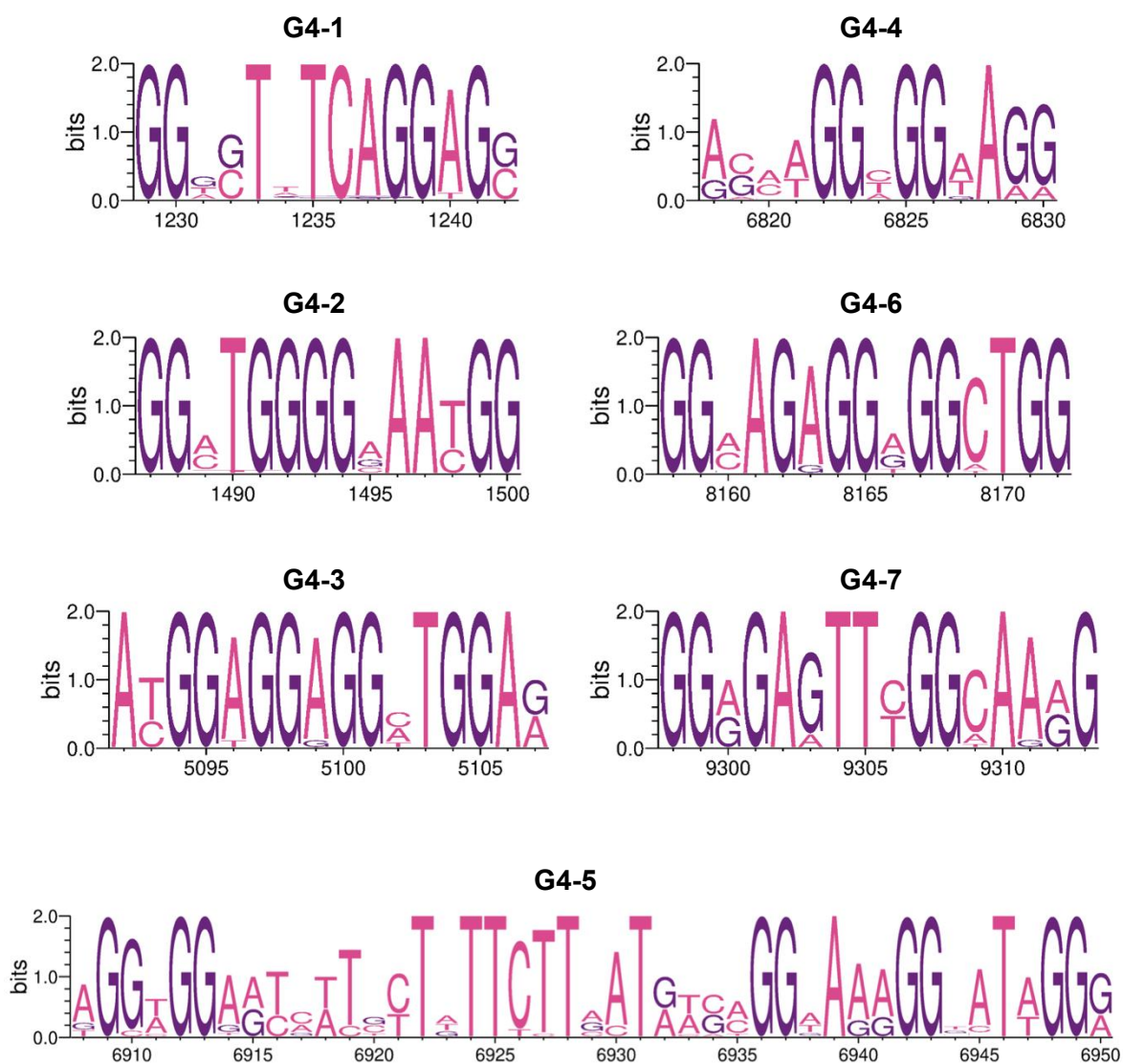


Figure S3. Large-scale analysis of G4 motif conservation across DENV sequences

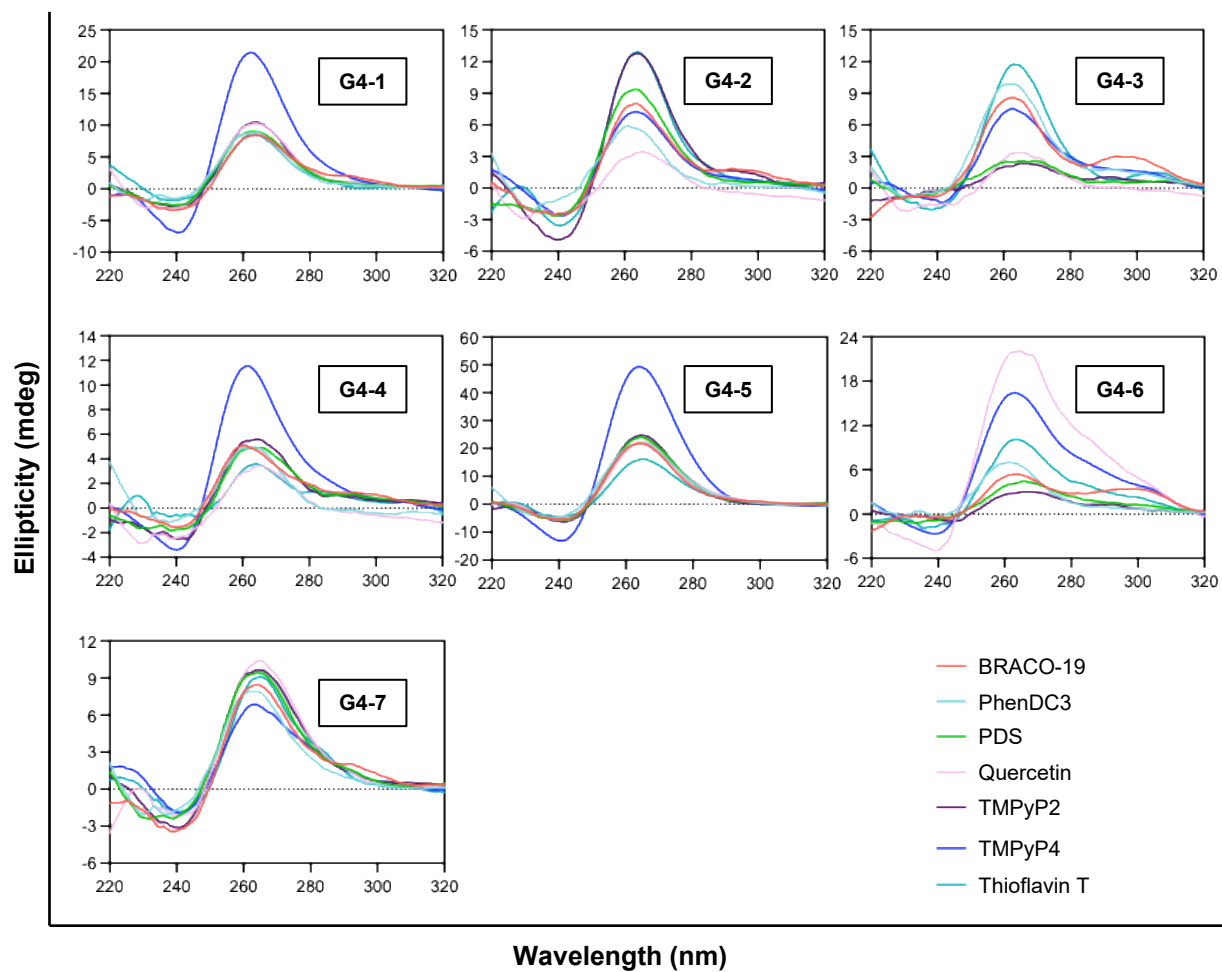


Figure S4. G4 topologies exhibit distinct CD signature

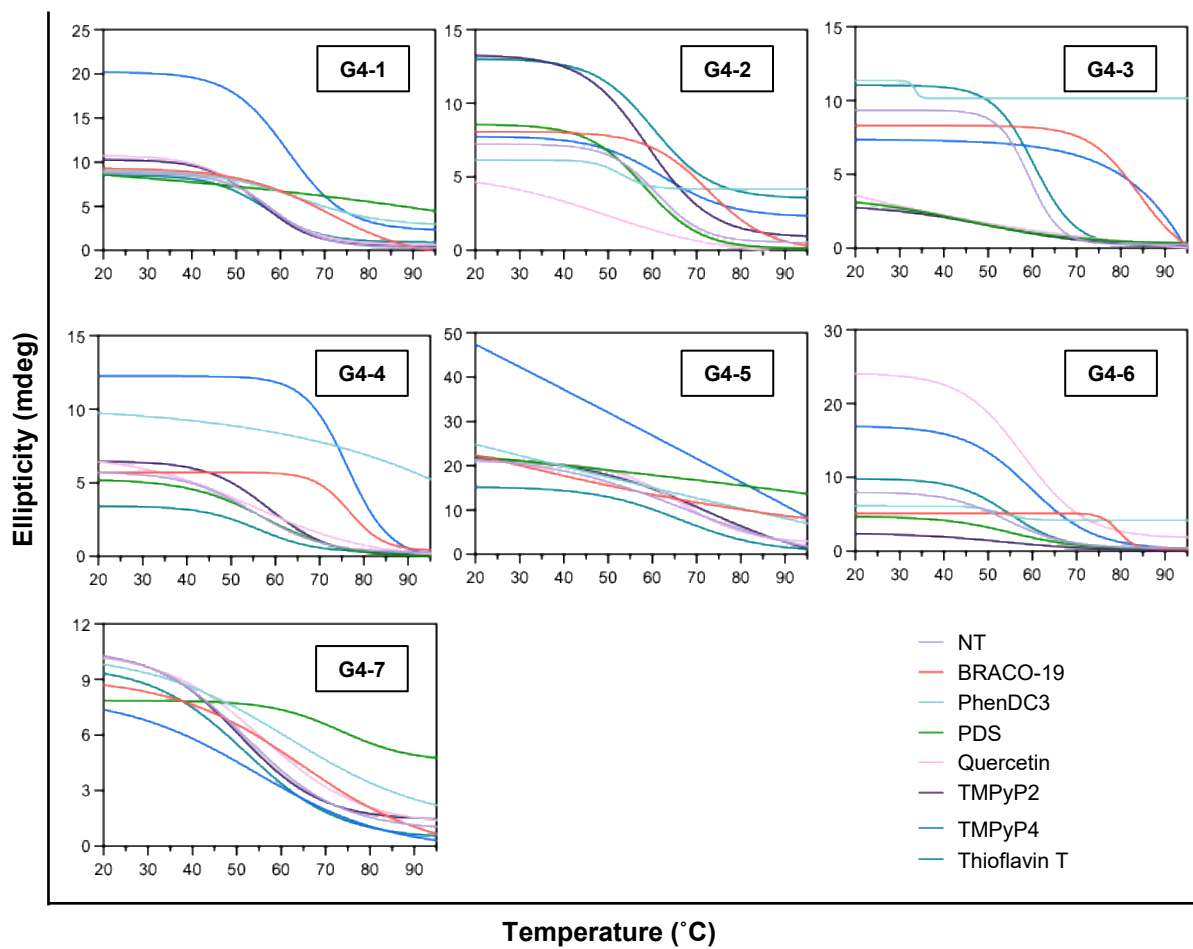


Figure S5. T_m analysis for G4 structures in presence of different G4 ligands

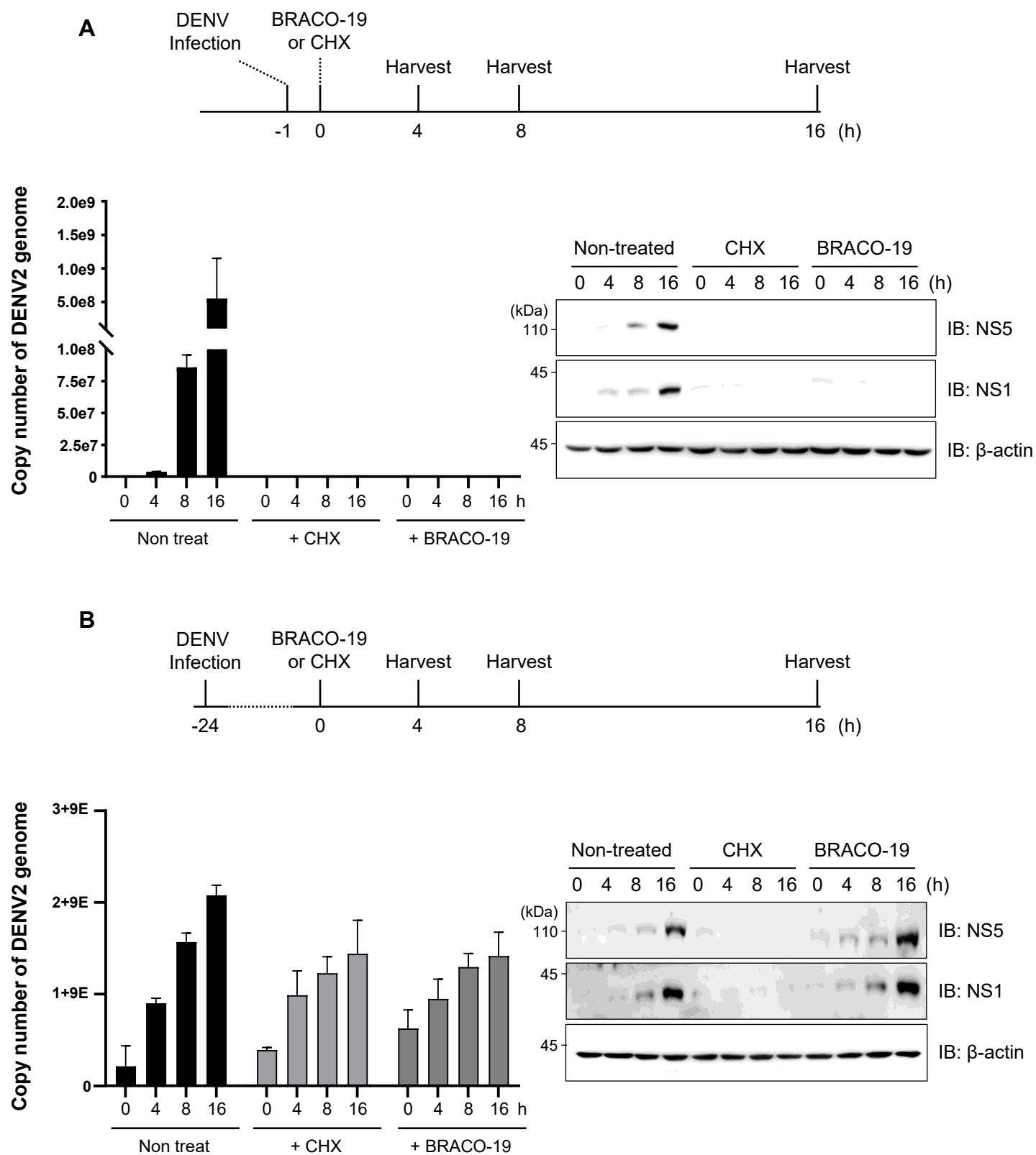


Figure S6. Cycloheximide chase analysis of BRACO-19-mediated translational inhibition of DENV2

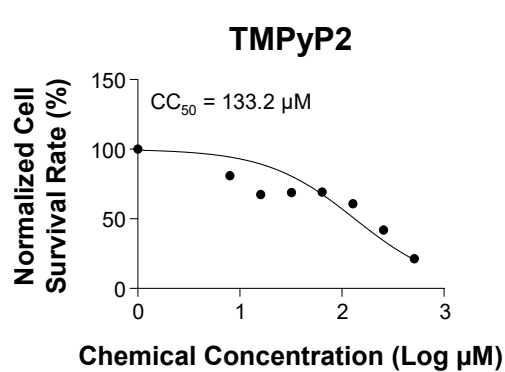
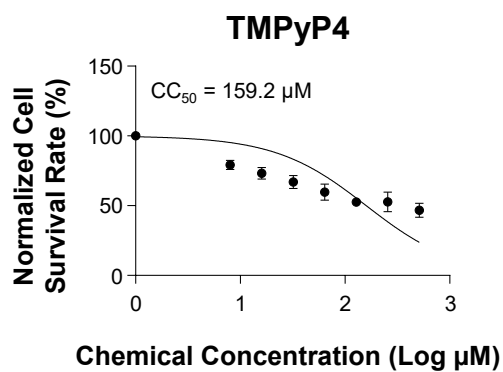
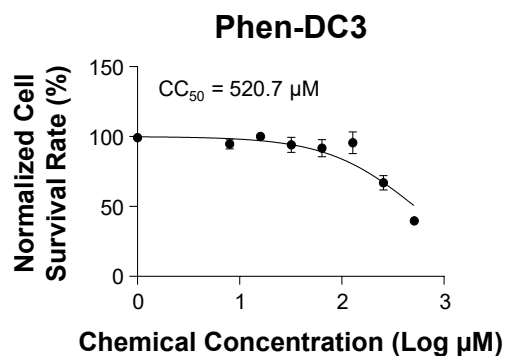
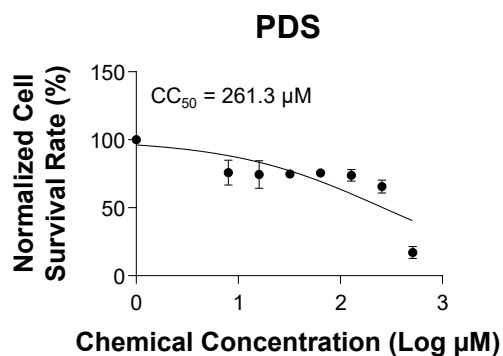
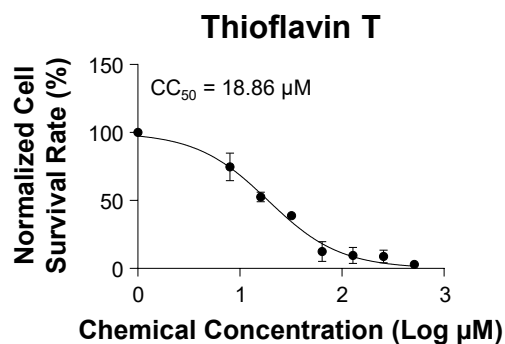
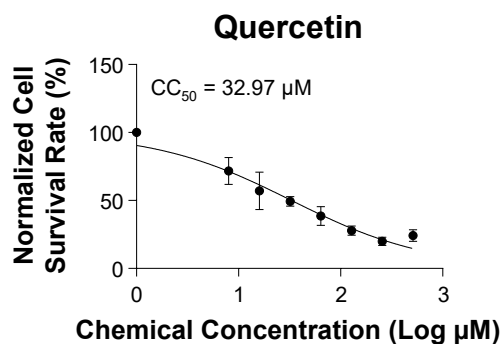


Figure S7. The cytotoxicity profile of G4 ligands

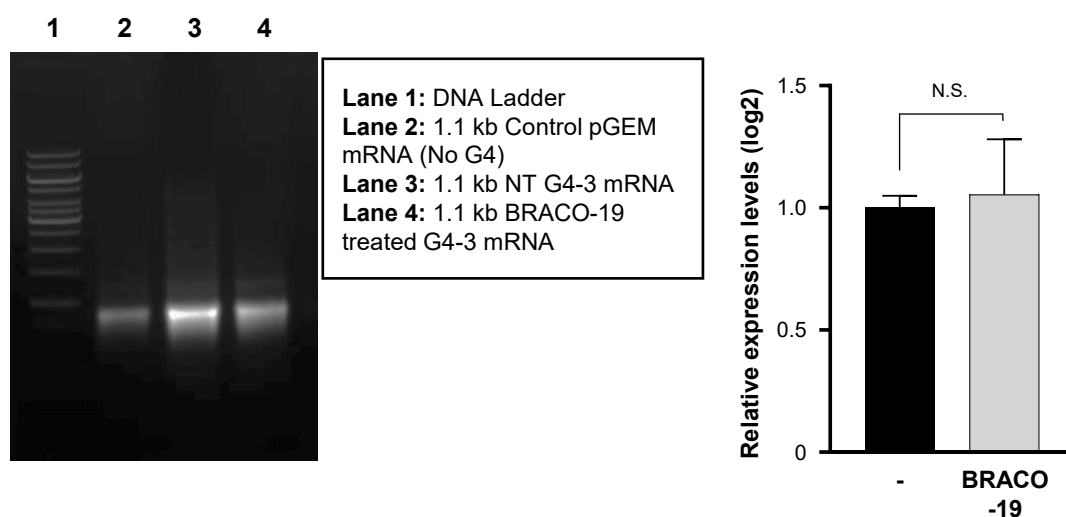


Figure S8. The effect of BRACO-19 on the transcription of the G4-containing reporter

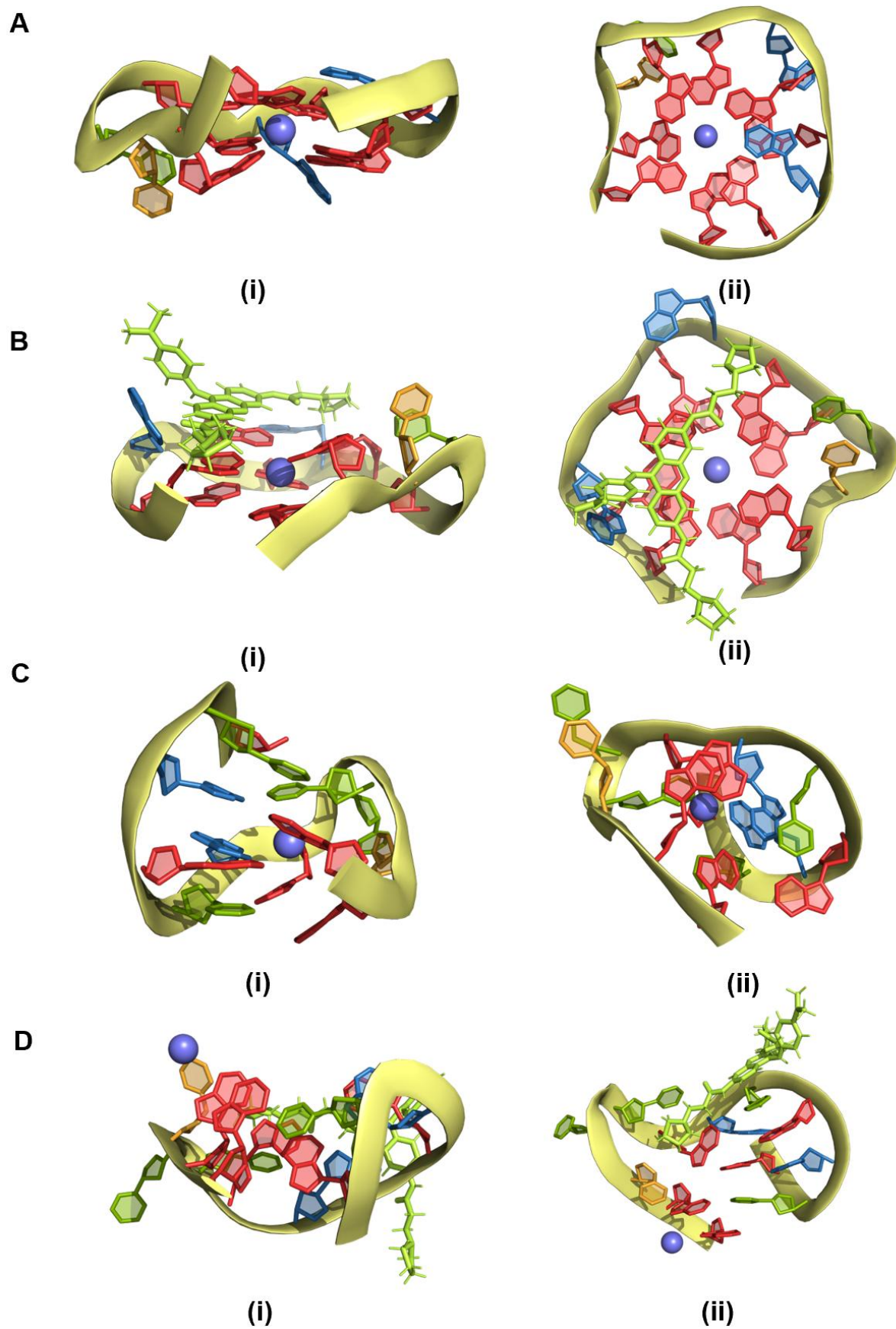


Figure S9. G4-3WT and G4-3 MT interaction analysis with BRACO-19

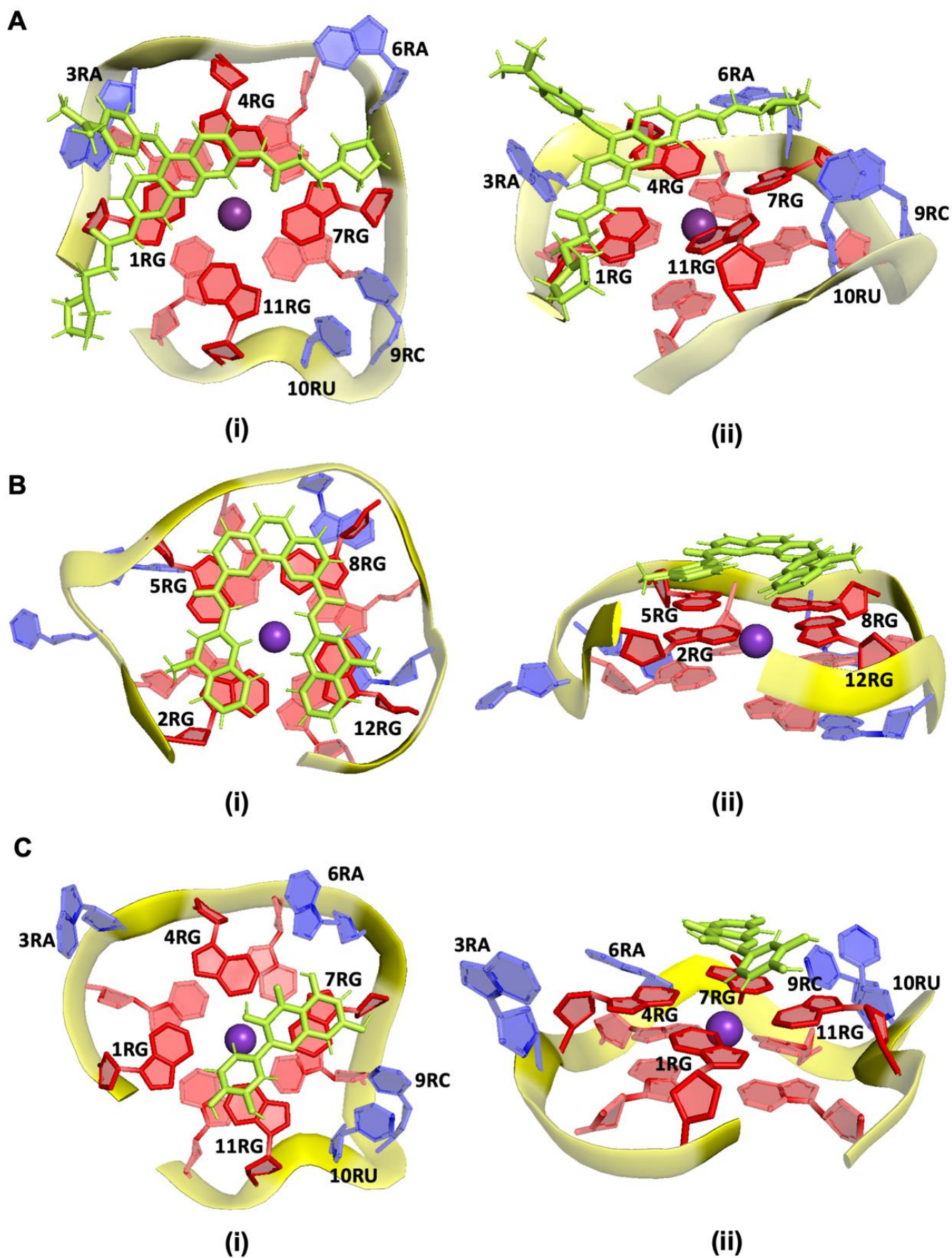


Figure S10. Comparing binding modes of Braco-19, PhenDC3 and Quercetin to G4-3

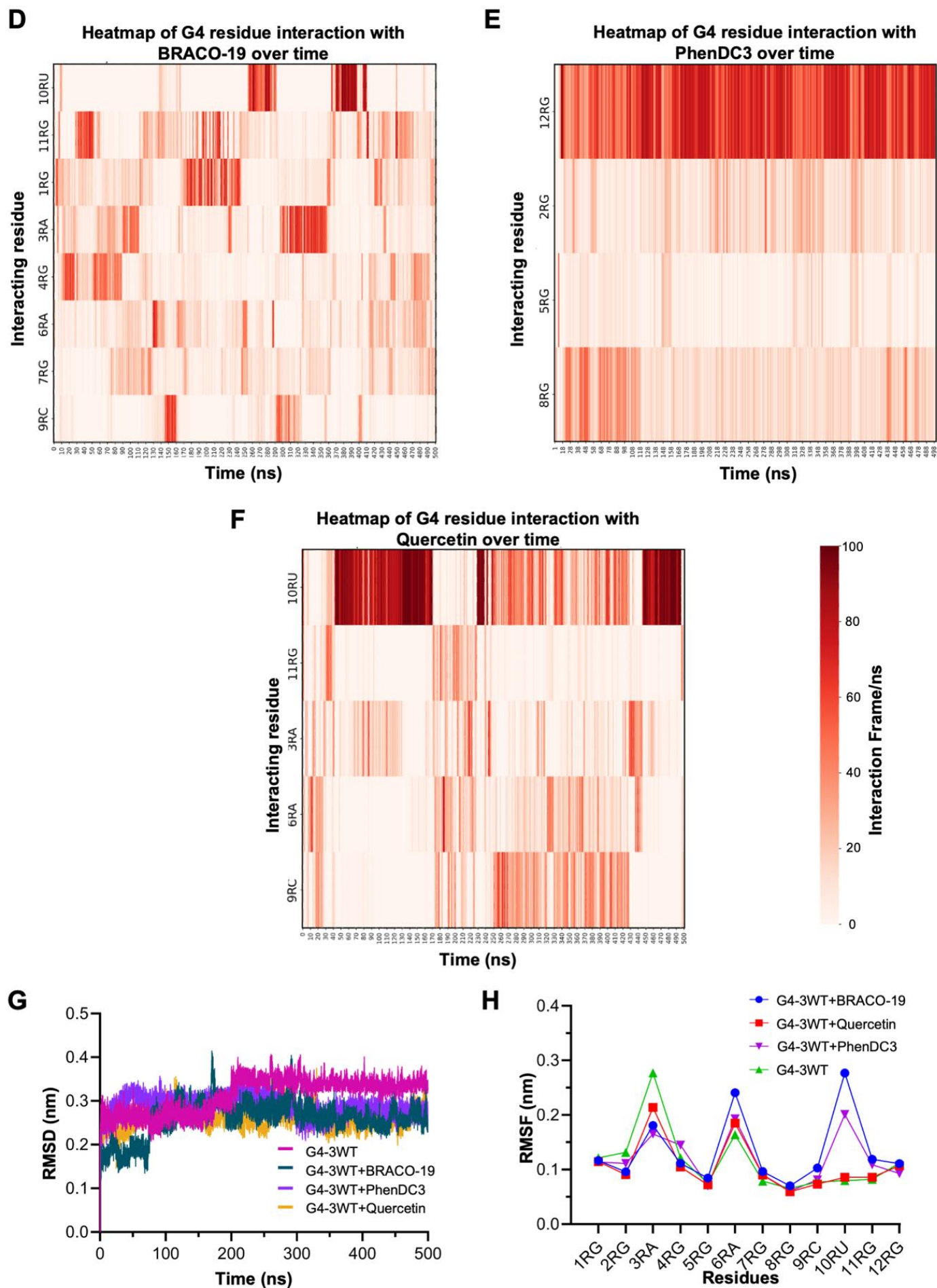


Figure S10. Comparing binding modes of Braco-19, PhenDC3 and Quercetin to G4-3

Sl. No	Start	End	Score	Strand	Sequence (5'-3')
1	976	989	29	+	GGGGTTTCAGGAGG
2	1234	1247	29	+	GGATGGGGAAATGG
3	2523	2537	27	-	CCAACCAGAATCCCC
4	4543	4556	29	-	CCTTCACCCCCACC
5	4759	4770	32	+	GGAGGAGGCTGG
6	5247	5259	30	-	CCAGACCCCAGCC
7	6480	6492	30	+	GGCAGGTGGAAGG
8	6570	6612	37	+	GGGAGGGATCTTTTATTCTTGATGAG CGGAAGGGGCATAGGG
9	7816	7830	27	+	GGCAGAGGAGGCTGG
10	8956	8971	26	+	GGGGAATTCGGCAAGG
11	10345	10360	26	-	CCTGTGAGCCCCGTCC

Table S1. Position and sequence of eleven G4 sequences screened using pqsfinder

Sl. No.	Name	RNA Sequence (5'-3')
1	G4-1	GGGGUUUCAGGAGG
2	G4-2	GGAUGGGGAAAUGG
3	G4-3	GGAGGAGGCUGG
4	G4-4	GGCAGGUGGAAGG
5	G4-5	GGGAGGGAUCUUUUUAUUCUUGAUGAG CGGAAGGGGCAUAGGG
6	G4-6	GGCAGAGGAGGCUGG
7	G4-7	GGGGAAUUCGGCAAGG
8	NRAS (Positive Control)	GGGAGGGGCGGGUCUGGG

Table S2. Sequence of the seven RNA G-quadruplex and positive control sequences used for further study

	Flaviviruses	Reference IDs
1	Absettarov virus	KJ000002.1
2	Aedes flavivirus	KC181923.1
3	Alkhumra hemorrhagic fever virus	AF331718.1
4	Aroa virus	KF917535.1
5	Bagaza virus	KR108246.1
6	Banzi virus	DQ859056.1
7	Barkedji virus	KC496020.1
8	Bouboui virus	DQ859057.1
9	Bussuquara virus	NC_009026.2
10	Cacipacore virus	NC_026623.1
11	Chaoyang virus	NC_017086.1
12	Culex theileri flavivirus	HE574574.1
13	Culiseta flavivirus	KT599442.1
14	Donggang virus	JQ086551.1
15	Edge Hill virus	DQ859060.1
16	Entebbe bat virus	DQ837641.1
17	Gadgets Gully virus	DQ235145.1
18	Hanko virus	JQ268258.1
19	Iguaape virus	AY632538.4
20	Ilheus virus	KC481679.1
21	Japanese encephalitis virus	L48961.1
22	Jugra virus	DQ859066.1
23	Kama virus	NC_023439.1
24	Kamiti River virus	NC_005064.1
25	Karshi virus	DQ462443.1
26	Kedougou virus	NC_012533.1
27	Kokobera virus	NC_009029.2
28	Koutango virus	OQ067500.1
29	Kyasanur Forest disease virus	AY323490.1
30	Lammi virus	FJ606789.2
31	Langat virus	NC_003690.1
32	Meaban virus	DQ235144.1
33	Modoc virus	AJ242984.1
34	Murray Valley encephalitis virus	NC_000943.1
35	Nakiwogo virus	GQ165809.1
36	Naranjal virus	KF917538.1
37	New Mapoon virus	KC788512.1
38	Nhumirim virus	NC_024017.1
39	Nienokoue virus	NC_024299.1
40	Nounane virus	EU159426.2
41	Ntaya virus	NC_018705.3
42	Omsk hemorrhagic fever virus	AY193805.1
43	Palm Creek virus	KC505248.1
44	Potiskum virus	DQ859067.1
45	Powassan virus	KU886216.1
46	Quang Binh virus	NC_012671.1
47	Rio bravo virus	NC_003675.1
48	Kadam virus from Uganda	NC_033724.1
49	Royal Farm virus	DQ235149.1
50	Saboya virus	DQ859062.1
51	Saumarez Reef virus	DQ235150.1
52	Sepik virus	NC_008719.1
53	Spondweni virus	NC_029055.1
54	Sokuluk virus	NC_026624.1
55	St. Louis encephalitis virus	NC_007580.2
56	Stratford virus	KF917540.1
57	Tamana bat virus	AF285080.1
58	Tick-borne encephalitis virus	NC_001672.1
59	Uganda S virus	DQ859065.1
60	Usutu virus	MT795154.1
61	Wesselsbron virus	NC_012735.1
62	West Nile virus	AY646354.1
63	Xishuangbanna aedes flavivirus	KU201526.1
64	Yaounde virus	EU082199.2
65	Yellow fever virus	NC_002031.1
66	Yokose virus	AB114858.1
67	Zika virus	NC_012532.1

Table S3. The panel of 67 flaviviruses used for G4 conservation analysis

Flaviviruses	Abbreviation	Reference IDs
Dengue virus serotype 1	DENV1	NC_001477.1
Dengue virus serotype 2	DENV2	NC_001474.2
Dengue virus serotype 3	DENV3	NC_001475.2
Dengue virus serotype 4	DENV4	NC_002640.1
Japanese encephalitis virus	JEV	L48961.1
West Nile virus	WNV	AY646354.1
Murray Valley encephalitis virus	MVEV	NC_000943.1
Zika virus	ZIKV	NC_012532.1
Yellow fever virus	YFV	NC_002031.1
Sepik virus	SEPV	NC_008719.1
Wesselsbron virus	WESSV	NC_012735.1
Tick-borne encephalitis virus	TBEV	NC_001672.1

Table S4. List of flaviviruses with their reference IDs used for G4 conservation analysis

Figure #	Virus	Titer (FFU/ml)
2	DENV2	5.0×10^5
3	DENV2	5.0×10^5
5	rDENV2-G4-3WT	2.0×10^6
	rDENV2-G4-3WT	1.0×10^6
6	DENV2	2.0×10^7 (Concentrated)

Table S5. Titer of DENV used in this study