

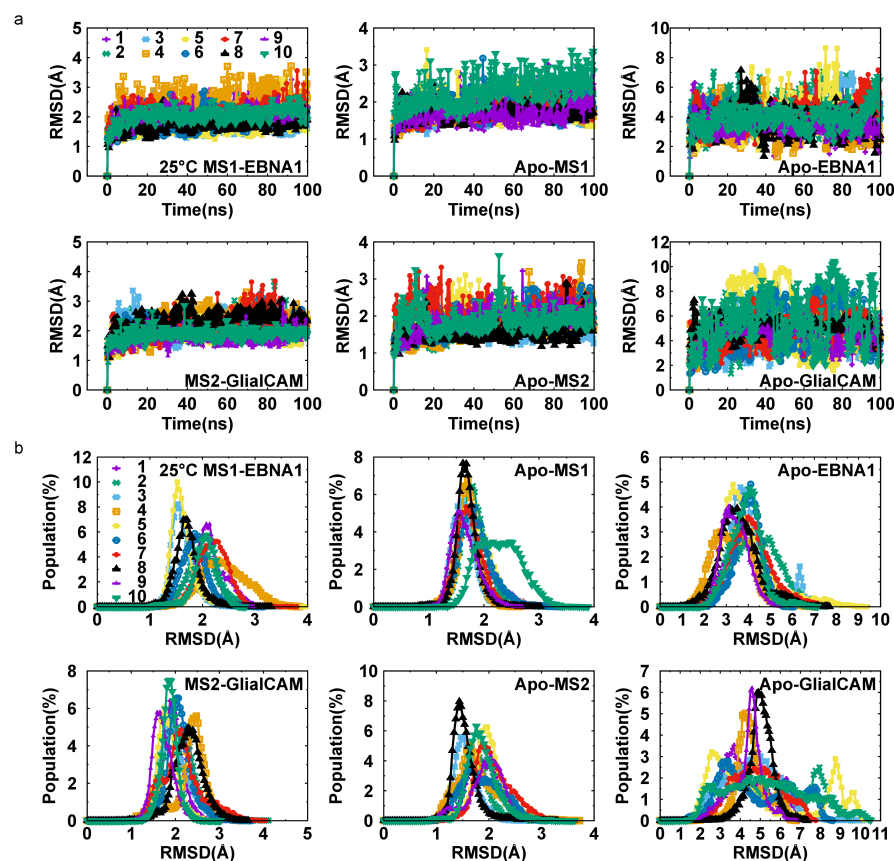


Figure S1: Root mean square deviations (RMSDs) of MS1-EBNA1, apo-MS1, apo-EBNA1, MS2-GliaCAM, apo-MS2 and apo-GliaCAM at 298K (25°). (a) RMSDs for simulation time (ns). (b) Distributions of RMSDs.

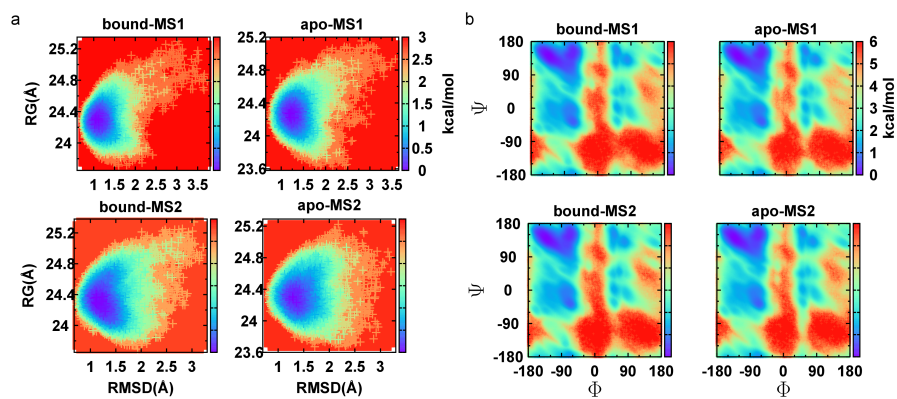
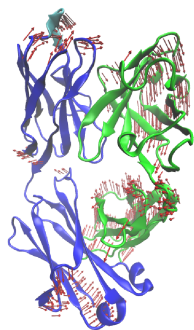
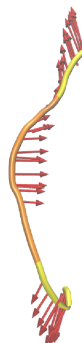


Figure S2: Tertiary and secondary structural differences for MS1 and MS2 in bound and apo states. (a) Free energy landscapes of MS1 and MS2 with respect to root mean square deviation (RMSD) and gyration radius (RG). (b) Free energy landscapes of MS1 and MS2 with respect to dihedral angles ϕ and ψ .

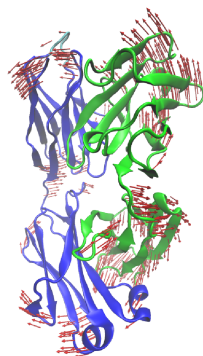
apo-MS1(23.34%)



apo-EBNA1(34.92%)



apo-MS2(22.89%)



apo-GlialCAM(45.77%)

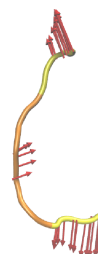


Figure S3: Tertiary and secondary structural differences for MS1 and MS2 in apo states. The most stable structures of apo-MS1, apo-EBNA1, apo-MS2 and apo-GlialCAM, where the front views are shown.

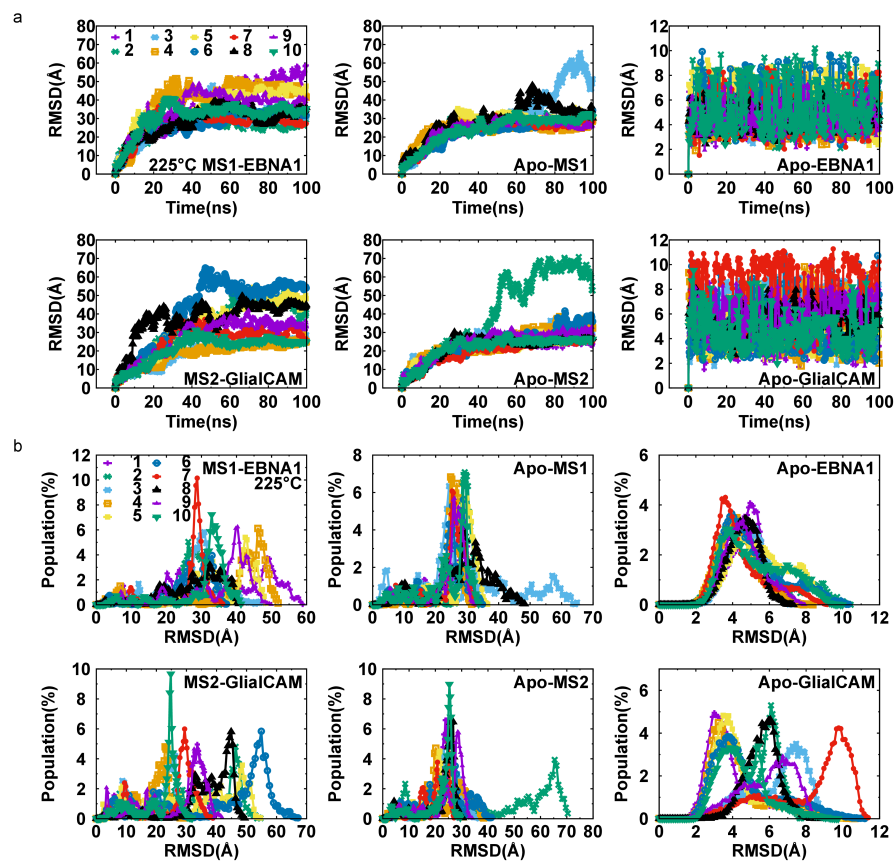


Figure S4: Root mean square deviations (RMSDs) of MS1-EBNA1, apo-MS1, apo-EBNA1, MS2-GlialCAM, apo-MS2 and apo-GlialCAM at 498K (225°). (a) RMSDs for simulation time (ns). (b) Distributions of RMSDs.

Table S1: Simulation Conditions for All Systems

Systems	Ions	Waters	Water Box Sizes ($\text{\AA}^3$)	Temperatures (K)	Time (ns)	Trajectories
MS1-EBNA1	8 Cl-	23,582	863,997	298 / 498	100	10
apo-MS1	5 Cl-	16,908	645,367	298 / 498	100	10
apo-EBNA1	3 Cl-	3,038	109,123	298 / 498	100	10
MS2-GlialCAM	7 Cl-	23,238	852,681	298 / 498	100	10
apo-MS2	5 Cl-	16,881	645,103	298 / 498	100	10
apo-GlialCAM	2 Cl-	3,595	125,615	298 / 498	100	10

Table S2: All Stable Interactions of MS1-EBNA1 with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages of Distances	Standard Errors
1	ligHrec	1	R437-P316	3.279	0.845
2	ligHrec	2	P439-Y275	3.595	0.269
3	ligHrec	3	R437-D315	3.599	1.582
4	ligHrec	4	P436-G96	3.843	1.050
5	ligHrec	5	R438-E273	3.881	1.658
6	ligHrec	6	R438-E273	3.910	1.628
7	ligHrec	7	R443-D278	3.912	2.365
8	ligHrec	8	R443-D278	3.914	2.371
9	ligHrec	9	R443-D1	4.002	2.771
10	ligHrec	10	R438-E273	4.007	1.475
11	ligHrec	11	R443-D1	4.027	2.771
12	ligHrec	12	R438-E273	4.056	1.462
13	ligHrec	13	R437-W249	4.111	0.341
14	ligHrec	14	R438-E273	4.184	1.494
15	ligHrec	15	R443-D278	4.229	2.314
16	ligHrec	16	P439-Y275	4.235	0.351
17	ligHrec	17	R443-D278	4.268	2.172
18	ligHrec	18	R443-D278	4.276	2.164
19	ligHrec	19	R438-E273	4.309	1.259
20	ligHrec	20	R437-W249	4.333	0.360
21	ligHrec	21	R437-W249	4.346	0.462
22	ligHrec	22	R443-D1	4.371	2.692
23	ligHrec	23	R437-D315	4.378	1.023
24	ligHrec	24	R437-P316	4.387	1.144
25	ligHrec	25	R437-P316	4.450	0.832
26	ligHrec	26	P436-G96	4.471	1.064
27	ligHrec	27	R443-D1	4.593	2.795
28	ligHrec	28	P436-G96	4.663	0.726
29	ligHrec	29	R443-D278	4.681	2.152
30	ligHrec	30	R443-D1	4.705	2.771
31	ligHrec	31	R437-D315	4.705	1.628
32	ligHrec	32	P436-G96	4.744	1.055
33	ligHrec	33	R437-W249	4.745	0.594
34	ligHrec	34	R437-W249	4.783	0.580
35	ligHrec	35	R443-D278	4.818	2.206
36	ligHrec	36	R443-D278	4.818	2.214
37	ligHrec	37	R437-D315	4.841	0.543
38	ligHrec	38	P436-Y31	4.842	0.711
39	ligHrec	39	P436-Y31	4.863	1.046
40	ligHrec	40	R438-E273	4.908	1.043
41	ligHrec	41	R438-E273	4.918	1.048
42	ligHrec	42	R437-P316	4.937	0.503
43	ligHrec	43	R443-D1	5.000	2.694

Table S2: All Stable Interactions of MS1-EBNA1 with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages of Distances	Standard Errors
44	ligHrec	44	R443-W99	5.003	2.185
45	ligHrec	45	P436-Y37	5.045	1.308
46	ligHrec	46	R437-D315	5.117	1.700
47	ligHrec	47	R437-W249	5.146	0.510
48	ligHrec	48	R437-W249	5.159	0.610
49	ligHrec	49	R437-P317	5.162	0.822
50	ligHrec	50	R443-D278	5.222	2.177
51	ligHrec	51	R438-E273	5.249	0.941
52	ligHrec	52	R443-D1	5.287	2.503
53	ligHrec	53	P436-G96	5.302	0.556
54	ligHrec	54	P436-Y31	5.356	1.308
55	ligHrec	55	P436-Y37	5.357	1.776
56	ligHrec	56	R443-P100	5.445	2.156
57	ligHrec	57	R443-D1	5.445	2.454
58	ligHrec	58	R437-P316	5.450	0.849
59	ligHrec	59	R438-W99	5.472	0.480
60	ligHrec	60	R443-W99	5.473	1.949
61	ligHrec	61	P436-G96	5.477	1.026
62	ligHrec	62	P435-P317	5.499	0.568
63	ligHrec	63	R437-P316	5.507	1.175
64	ligHrec	64	R443-P100	5.535	2.162
65	ligHrec	65	R443-W99	5.538	2.120
66	ligHrec	66	P439-Y275	5.546	0.337
67	ligHrec	67	P436-G96	5.580	0.736
68	ligHrec	68	P435-Y37	5.582	0.749
69	ligHrec	69	R437-D315	5.583	1.018
70	ligHrec	70	R443-W99	5.615	1.795
71	ligHrec	71	R437-W249	5.646	0.843
72	ligHrec	72	P435-P316	5.668	0.945
73	ligHrec	73	R438-Y275	5.687	0.341
74	ligHrec	74	R437-P316	5.706	0.344
75	ligHrec	75	R437-D315	5.717	0.909
76	ligHrec	76	R443-D1	5.762	2.384
77	ligHrec	77	R437-W249	5.782	0.616
78	ligHrec	78	R443-W99	5.830	1.979
79	ligHrec	79	P439-Y275	5.897	0.258
80	ligHrec	80	R438-W99	5.917	0.471
81	ligHrec	81	P435-P316	5.922	0.981
82	ligHrec	82	R437-P317	5.928	0.364
83	ligHrec	83	R443-P100	5.955	1.903
84	ligHrec	84	R443-W99	5.978	1.666
85	ligHrec	85	P435-Y37	5.999	0.535
86	ligHrec	86	R437-D315	6.005	0.558

Table S2: All Stable Interactions of MS1-EBNA1 with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages of Distances	Standard Errors
87	ligHrec	87	R443-W99	6.014	1.794
88	ligHrec	88	R443-W99	6.019	1.849
89	ligHrec	89	R437-P316	6.019	0.339
90	ligHrec	90	R437-D315	6.038	1.348
91	ligHrec	91	P436-Y31	6.072	1.026
92	ligHrec	92	P435-P316	6.089	0.734
93	ligHrec	93	P435-P317	6.100	0.634
94	ligHrec	94	R437-P317	6.104	1.222
95	ligHrec	95	R437-P316	6.110	0.520
96	ligHrec	96	R437-D315	6.136	0.921
97	ligHrec	97	P439-Y276	6.195	0.607
98	ligHrec	98	P439-Y275	6.217	0.423
99	ligHrec	99	R437-P316	6.259	1.170
100	ligHrec	100	R437-D315	6.269	1.453
101	ligHrec	101	R438-N266	6.288	0.443
102	ligHrec	102	R437-D315	6.328	1.020
103	ligHrec	103	P435-Y31	6.329	0.695
104	ligHrec	104	P439-Y275	6.339	0.479
105	ligHrec	105	P436-G96	6.387	0.553
106	ligHrec	106	P436-P317	6.388	0.771
107	ligHrec	107	P435-Y37	6.403	1.213
108	ligHrec	108	P436-P317	6.422	0.468
109	ligHrec	109	R437-D315	6.470	0.588
110	ligHrec	110	R443-W99	6.484	1.722
111	ligHrec	111	P435-P317	6.491	0.408
112	ligHrec	112	R438-W249	6.497	2.072
113	recHlig	1	Y31-S434	4.050	1.130
114	recHlig	2	P317-P436	4.138	0.633
115	recHlig	3	P317-P436	4.199	0.675
116	recHlig	4	P317-P436	4.301	0.666
117	recHlig	5	Y31-P436	4.598	0.873
118	recHlig	6	P317-P436	4.750	0.502
119	recHlig	7	P317-P436	4.773	0.437
120	recHlig	8	Y31-P435	4.801	0.849
121	recHlig	9	P317-P436	4.826	0.490
122	recHlig	10	Y37-P435	4.913	1.227
123	recHlig	11	Y31-S434	4.950	1.080
124	recHlig	12	P317-P436	4.955	0.471
125	recHlig	13	P317-P435	4.961	0.388
126	recHlig	14	P317-P435	5.051	0.522
127	recHlig	15	Y31-P435	5.118	0.972
128	recHlig	16	P317-P436	5.128	0.698
129	recHlig	17	R35-G433	5.184	1.873

Table S2: All Stable Interactions of MS1-EBNA1 with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages of Distances	Standard Errors
130	recHlig	18	P317-P436	5.234	0.533
131	recHlig	19	R35-G433	5.244	1.965
132	recHlig	20	P317-P435	5.280	0.651
133	recHlig	21	R35-G433	5.369	1.277
134	recHlig	22	Y37-S434	5.383	1.482
135	recHlig	23	Y31-P435	5.458	1.121
136	recHlig	24	Y37-G433	5.459	1.995
137	recHlig	25	Y37-S434	5.490	1.781
138	recHlig	26	Y318-P435	5.541	0.709
139	recHlig	27	R35-G433	5.558	1.859
140	recHlig	28	Y37-P435	5.611	1.334
141	recHlig	29	P317-P435	5.629	0.799
142	recHlig	30	P317-P436	5.685	0.566
143	recHlig	31	R35-G433	5.750	1.985
144	recHlig	32	P316-P436	5.778	0.726
145	recHlig	33	Y37-P436	5.814	1.612
146	recHlig	34	R35-S432	5.857	1.710
147	recHlig	35	R35-G433	5.947	1.317
148	recHlig	36	R35-S432	5.996	1.825
149	recHlig	37	P317-P436	6.050	0.506
150	recHlig	38	Y31-P436	6.057	1.105
151	recHlig	39	Y275-P439	6.060	0.435
152	recHlig	40	R35-S432	6.114	2.083
153	recHlig	41	R35-S432	6.132	2.283
154	recHlig	42	P316-P436	6.140	0.711
155	recHlig	43	P317-P435	6.149	0.406
156	recHlig	44	P317-P435	6.166	0.527
157	recHlig	45	Y37-G433	6.198	1.965
158	recHlig	46	Y275-R438	6.264	0.430
159	recHlig	47	G96-P436	6.373	0.478
160	recHlig	48	P317-P435	6.391	0.595
161	recHlig	49	Y31-G433	6.395	1.770
162	recHlig	50	Y31-G433	6.428	1.516
163	recHlig	51	R35-S432	6.435	1.567
164	recHlig	52	Y318-P435	6.466	0.671
165	recHlig	53	Y275-R437	6.491	0.380
166	hy	1	W99-P439	4.405	0.255
167	hy	2	Y31-P436	4.478	0.939
168	hy	3	Y275-P439	4.616	0.345
169	hy	4	P317-P436	5.194	0.835
170	hy	5	Y37-P436	5.498	1.757
171	hy	6	Y37-P435	5.543	0.762
172	hy	7	P317-P435	5.628	0.572

Table S2: All Stable Interactions of MS1-EBNA1 with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages of Distances	Standard Errors
173	hy	8	Y318-P435	5.758	0.578
174	hy	9	W99-P440	5.784	0.420
175	ele	1	E273-R438	4.916	0.872
176	ele	2	D278-R443	4.984	1.938
177	ele	3	D1-R443	5.994	2.289
178	ele	4	D315-R437	6.020	0.673
179	ele	5	E273-R437	9.693	1.023

Table S3: All Stable Interactions of MS2-GlialCAM with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages	Standard Errors
1	ligHrec	1	R437-P316	3.118	0.660
2	ligHrec	2	P436-G96	3.499	0.344
3	ligHrec	3	R437-D315	3.761	1.454
4	ligHrec	4	P439-Y275	3.868	0.431
5	ligHrec	5	R437-W249	4.078	0.320
6	ligHrec	6	P436-G96	4.124	0.560
7	ligHrec	7	R437-P316	4.197	0.931
8	ligHrec	8	R437-P316	4.276	0.636
9	ligHrec	9	R437-W249	4.362	0.375
10	ligHrec	10	R437-W249	4.394	0.459
11	ligHrec	11	P436-G96	4.404	0.331
12	ligHrec	12	A438-Y275	4.447	0.347
13	ligHrec	13	A438-Y275	4.502	0.517
14	ligHrec	14	P436-G96	4.538	0.493
15	ligHrec	15	R437-D315	4.572	1.500
16	ligHrec	16	P439-Y275	4.682	0.560
17	ligHrec	17	R437-D315	4.690	1.790
18	ligHrec	18	R437-D315	4.690	1.104
19	ligHrec	19	P436-Y37	4.740	0.731
20	ligHrec	20	R437-W249	4.845	0.637
21	ligHrec	21	P436-Y37	4.932	0.983
22	ligHrec	22	R437-P317	4.934	0.604
23	ligHrec	23	R437-W249	4.944	0.593
24	ligHrec	24	R437-P316	4.969	0.451
25	ligHrec	25	P436-Y31	5.014	1.572
26	ligHrec	26	P436-G96	5.119	0.500
27	ligHrec	27	P436-Y31	5.119	1.594
28	ligHrec	28	P436-G96	5.137	0.387
29	ligHrec	29	R437-W249	5.177	0.556
30	ligHrec	30	R437-P316	5.298	0.941
31	ligHrec	31	R437-W249	5.306	0.616
32	ligHrec	32	R437-D315	5.351	0.886
33	ligHrec	33	R437-P316	5.367	0.712
34	ligHrec	34	P435-P317	5.392	0.380
35	ligHrec	35	A438-Y275	5.396	0.394
36	ligHrec	36	P436-G96	5.461	0.479
37	ligHrec	37	P435-P316	5.462	0.514
38	ligHrec	38	R437-D315	5.495	0.952
39	ligHrec	39	P436-Y31	5.545	1.630
40	ligHrec	40	R437-D315	5.598	0.776
41	ligHrec	41	R437-P316	5.687	0.380
42	ligHrec	42	R437-W249	5.770	0.793
43	ligHrec	43	R437-P317	5.813	0.389

Table S3: All Stable Interactions of MS2-GliaCAM with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages	Standard Errors
44	ligHrec	44	R437-P317	5.826	0.935
45	ligHrec	45	P435-Y37	5.832	0.621
46	ligHrec	46	R437-D315	5.858	1.368
47	ligHrec	47	R437-W249	5.867	0.618
48	ligHrec	48	R437-D315	5.890	1.191
49	ligHrec	49	P435-P316	5.939	0.429
50	ligHrec	50	R437-P316	5.943	0.369
51	ligHrec	51	P435-P316	5.957	0.697
52	ligHrec	52	R437-D315	5.981	0.777
53	ligHrec	53	P439-Y275	6.007	0.505
54	ligHrec	54	R437-D315	6.061	1.259
55	ligHrec	55	R437-P316	6.120	0.455
56	ligHrec	56	P435-Y37	6.123	0.570
57	ligHrec	57	P436-P317	6.148	0.330
58	ligHrec	58	R437-P316	6.158	1.030
59	ligHrec	59	P439-Y275	6.167	0.384
60	ligHrec	60	R437-D315	6.200	0.706
61	ligHrec	61	P436-G96	6.204	0.358
62	ligHrec	62	P435-P317	6.234	0.528
63	ligHrec	63	P439-Y276	6.295	0.765
64	ligHrec	64	P436-P317	6.314	0.400
65	ligHrec	65	R437-W99	6.318	0.591
66	ligHrec	66	P436-Y37	6.334	0.896
67	ligHrec	67	R437-D315	6.341	1.048
68	ligHrec	68	P436-Y31	6.386	1.573
69	ligHrec	69	P439-Y275	6.390	0.491
70	ligHrec	70	P436-P317	6.404	0.460
71	ligHrec	71	P435-P317	6.421	0.336
72	ligHrec	72	R437-Y318	6.444	1.342
73	ligHrec	73	R437-G96	6.487	0.535
74	ligHrec	74	P435-Y318	6.493	0.407
75	recHlig	1	Y31-S434	3.633	1.479
76	recHlig	2	P317-P436	4.147	0.585
77	recHlig	3	P317-P436	4.188	0.592
78	recHlig	4	P317-P436	4.255	0.652
79	recHlig	5	P317-P436	4.587	0.414
80	recHlig	6	Y31-P436	4.598	1.405
81	recHlig	7	Y37-P435	4.691	0.834
82	recHlig	8	Y31-S434	4.729	1.355
83	recHlig	9	P317-P436	4.744	0.459
84	recHlig	10	P317-P436	4.744	0.412
85	recHlig	11	Y31-P435	4.810	1.432
86	recHlig	12	P317-P436	4.834	0.340

Table S3: All Stable Interactions of MS2-GliaCAM with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages	Standard Errors
87	recHlig	13	P317-P435	4.932	0.356
88	recHlig	14	P317-P436	5.010	0.620
89	recHlig	15	P317-P435	5.014	0.454
90	recHlig	16	P317-P436	5.061	0.485
91	recHlig	17	Y31-P435	5.155	1.507
92	recHlig	18	Y37-S434	5.242	0.957
93	recHlig	19	Y37-P435	5.363	0.904
94	recHlig	20	Y37-S434	5.363	1.100
95	recHlig	21	P317-P435	5.390	0.453
96	recHlig	22	Y31-P435	5.436	1.330
97	recHlig	23	P317-P436	5.467	0.476
98	recHlig	24	Y37-P436	5.485	1.037
99	recHlig	25	Y37-S433	5.539	1.225
100	recHlig	26	P316-P436	5.712	0.611
101	recHlig	27	P317-P435	5.726	0.526
102	recHlig	28	Y31-S433	5.808	1.377
103	recHlig	29	Y318-P435	5.821	0.690
104	recHlig	30	P317-P436	5.889	0.457
105	recHlig	31	Y275-P439	6.071	0.544
106	recHlig	32	P317-P435	6.088	0.483
107	recHlig	33	P316-P436	6.098	0.623
108	recHlig	34	Y31-S433	6.136	1.536
109	recHlig	35	G96-P436	6.159	0.417
110	recHlig	36	Y31-P436	6.164	1.463
111	recHlig	37	Y275-A438	6.180	0.463
112	recHlig	38	Y275-R437	6.218	0.432
113	recHlig	39	P317-P435	6.222	0.356
114	recHlig	40	Y37-S433	6.297	1.074
115	recHlig	41	Y37-P435	6.429	0.812
116	recHlig	42	P316-P436	6.455	0.494
117	recHlig	43	P317-P435	6.466	0.449
118	hy	1	Y275-A438	3.957	0.384
119	hy	2	W99-P439	4.450	0.539
120	hy	3	Y31-P436	4.594	1.512
121	hy	4	P317-P436	4.930	0.382
122	hy	5	Y275-P439	4.945	0.566
123	hy	6	Y37-P436	5.090	1.008
124	hy	7	Y37-P435	5.693	0.604
125	hy	8	P317-P435	5.734	0.465
126	hy	9	Y318-P435	5.872	0.508
127	hy	10	W99-A438	6.280	0.419
128	ele	1	D315-R437	6.022	0.725
129	ele	2	D33-R430	10.398	5.025

Table S3: All Stable Interactions of MS2-GlialCAM with Residue-to-Residue Distances

Numbers	Groups	Group-Numbers	Residues	Averages	Standard Errors
130	ele	3	E273-R437	10.554	1.221