Biophysical and dynamic characterization of a fine-tuned binding of the human Respiratory Syncytial Virus M2-1 core domain to long RNAs

Icaro P. Caruso[1,2,3], Giovana C. Guimarães[1], Vitor B. Machado[1], Marcelo A. Fossey[1,2], Dieter Willbold[4], Fabio C. L. Almeida[3,*], Fátima P. Souza[1,2,*]

[1]Multiuser Center for Biomolecular Innovation (CMIB), [2]Department of Physics, IBILCE/UNESP, 15054-000, São José do Rio Preto, SP, Brazil;

[3]National Center for Nuclear Magnetic Resonance of Macromolecules, Institute of Medical Biochemistry Leopoldo de Meis (IBqM) and National Center for Structural Biology and Bioimaging (CENABIO), UFRJ, 21941-590 Rio de Janeiro, RJ, Brazil

[4]Institute of Biological Information Processing, Structural Biochemistry and JuStruct (IBI-7), Forchungszentrum Jülich, 52425 Jülich; Institut für Physikalische Biologie, Heinrich-Heine-Universität Düsseldorf, Universitätsstraße, 40225 Düsseldorf, Germany.

[*]Corresponding author e-mail address: falmeida@bioqmed.ufrj.br

fatima.p.souza@unesp.br

Tel.: +55-21-31042326

Tel.: +55-17-32212240

SUPPLEMENTARY MATERIAL

Table S1. Raw nuclear spin relaxation data (^{15}N R_1, R_2 and hetNOE) of the cdM2-1 backbone in its free and RNA-bound state. [cdM2-1] = 350 μM, [RNA] = 115 μM, 25 °C, and 14.1 T (^{1}H frequency of 600 MHz).

Res	cdM2-1						cdM2-1 + RNA					
	R_1	$\pm R_1$	R_2	$\pm R_2$	hNOE	$\pm$hNOE	R_1	$\pm R_1$	R_2	$\pm R_2$	hNOE	$\pm$hNOE
59	1.195	0.019	1.86	0.34	-0.871	0.009	1.181	0.016	2.23	0.352	-0.79	0.008
60	1.268	0.009	1.734	0.173	-0.53	0.008	1.248	0.016	2.097	0.186	-0.483	0.008
61	1.318	0.02	2.363	0.336	-0.609	0.01	1.273	0.027	2.839	0.358	-0.572	0.009
62	1.281	0.021	2.402	0.38	-0.409	0.012	1.207	0.016	2.56	0.421	-0.412	0.011
63	1.323	0.017	2.422	0.31	-0.285	0.006	1.315	0.016	2.863	0.32	-0.214	0.006
64	1.362	0.012	2.639	0.242	-0.239	0.006	1.325	0.011	3.079	0.224	-0.252	0.006
65	1.455	0.011	3.299	0.158	-0.173	0.007	1.411	0.01	3.606	0.161		
66	1.498	0.006	3.797	0.074	0.086	0.007	1.439	0.007	4.384	0.107	0.038	0.007
67	1.574	0.006	4.355	0.116	0.083	0.007	1.481	0.009	6.002	0.175		
68	1.546	0.013	4.703	0.162	0.212	0.009	1.482	0.016	5.685	0.189	0.18	0.009
69	1.58	0.016	5.822	0.203	0.275	0.009	1.493	0.016	7.737	0.232	0.224	0.011
70	1.609	0.013	6.446	0.167	0.369	0.009	1.502	0.012	8.836	0.212	0.335	0.012
71	1.569	0.01	6.821	0.256	0.344	0.01						
72	1.509	0.006	8.559	0.155	0.505	0.009						
73	1.549	0.017	8.558	0.185	0.429	0.013	1.397	0.013	12.708	0.271	0.413	0.018
74	1.364	0.008	7.611	0.144	0.44	0.013	1.17	0.019	14.811	0.266	0.561	0.032
75	1.409	0.015	9.365	0.121	0.727	0.02	1.232	0.012	15.775	0.323	0.702	0.039
76	1.396	0.006	10.486	0.163	0.732	0.021	1.124	0.02	21.211	0.606	0.738	0.056
77	1.381	0.005	11.199	0.117	0.83	0.022	1.06	0.024	21.544	0.894	0.889	0.068
78	1.432	0.007	11.255	0.1	0.773	0.021	1.108	0.029	20.676	0.648	0.805	0.062
79	1.453	0.015	11.819	0.13	0.827	0.027	1.198	0.046	24.589	1.341	0.753	0.076
80	1.452	0.01	11.458	0.092	0.803	0.022	1.082	0.034	20.547	1.177	0.862	0.094
81	1.433	0.012	10.951	0.07	0.796	0.018	1.127	0.021	20.444	1.018	0.79	0.076
82	1.465	0.006	11.709	0.164	0.767	0.016	1.137	0.022	23.437	0.716	0.682	0.056
83	1.505	0.009	10.96	0.088	0.749	0.017	1.19	0.022	20.399	0.954	0.889	0.067
84	1.452	0.012	14.922	0.123	0.798	0.024	1.224	0.042	24.88	1.925	0.848	0.093
85	1.461	0.009	10.962	0.138	0.761	0.017	1.174	0.025	19.923	0.644	0.844	0.056
86	1.479	0.008	10.73	0.166	0.761	0.016	1.16	0.027	20.553	0.84	0.738	0.05
87	1.421	0.009	16.194	0.169	0.77	0.023	1.14	0.023	24.944	0.574	0.792	0.059
88	1.463	0.016	16.649	0.261	0.739	0.026	1.122	0.035	27.645	1.304	0.659	0.077
89	1.449	0.016	12.658	0.263	0.708	0.017	1.165	0.017	20.489	0.72	0.713	0.045
90	1.278	0.008	11.008	0.161	0.649	0.019						
91					0.754	0.02						
92	1.437	0.021	11.59	0.244	0.836	0.024	1.051	0.089	22.116	2.475	1.091	0.215
93	1.429	0.008	11.589	0.165	0.775	0.017						
94	1.45	0.007	11.087	0.223	0.795	0.017	1.042	0.035	22.841	1.288	0.69	0.072
95	1.443	0.01	11.717	0.157	0.783	0.02	1.112	0.016	23.941	0.777	0.703	0.063
96					0.809	0.018						
97	1.407	0.006	11.337	0.117	0.741	0.017	1.035	0.032	21.201	1.056	0.584	0.063
98	1.458	0.011	11.755	0.144	0.783	0.022	1.13	0.038	23.609	0.842	0.753	0.066
99	1.395	0.006	11.445	0.103	0.767	0.014						
100	1.339	0.003	9.865	0.14	0.767	0.016					0.576	0.047
101	1.429	0.006	11.639	0.106	0.776	0.017	1.091	0.028	23.224	0.936	0.807	0.07
102	1.398	0.01	10.866	0.141	0.793	0.018	1.095	0.023	23.316	0.781	0.688	0.068
103	1.406	0.006	11.872	0.093	0.796	0.02	1.057	0.036	23.601	1.262	0.792	0.085
104	1.423	0.008	10.45	0.129	0.66	0.013					0.543	0.033
105	1.443	0.008	10.976	0.109	0.735	0.015	1.082	0.027	22.394	0.573	0.663	0.05
106					0.737	0.009						
107	1.312	0.008	9.355	0.096	0.714	0.018	1.036	0.023	18.079	0.54	0.641	0.05
108	1.42	0.02	11.696	0.274	0.763	0.023	1.073	0.035	21.578	0.77	0.859	0.082

109	1.422	0.007	11.269	0.207	0.762	0.013	1.126	0.011	21.998	0.343	0.823	0.036
110	1.288	0.006	11.286	0.142	0.728	0.015	1.025	0.009	21.932	0.448	0.768	0.051
111					0.737	0.009						
112	1.409	0.006	11.449	0.106	0.769	0.017	1.169	0.026	23.162	0.892	0.744	0.054
113	1.338	0.005	11.633	0.089	0.75	0.013	1.061	0.015	22.239	0.458	0.762	0.046
114	1.327	0.006	11.453	0.09	0.72	0.016	1.053	0.02	20.789	0.641	0.82	0.062
115	1.389	0.005	11.68	0.129	0.771	0.017	1.113	0.013	20.01	0.649	0.682	0.053
116	1.391	0.005	11.556	0.091	0.755	0.014						
117					0.738	0.014	0.992	0.019	21.981	0.379	0.729	0.043
118	1.361	0.006	10.103	0.092	0.752	0.013	1.066	0.016	20.018	0.393	0.739	0.037
119	1.283	0.006	10.73	0.065	0.603	0.013	1.034	0.019	19.743	0.619	0.565	0.041
121	1.347	0.01	10.719	0.229	0.698	0.022	1.047	0.025	19.657	0.515	0.526	0.056
122	1.385	0.005	10.518	0.085	0.705	0.011						
124	1.386	0.005	11.424	0.14	0.717	0.016	1.079	0.018	23.542	0.649	0.671	0.053
125	1.387	0.007	11.365	0.13	0.739	0.016	1.073	0.033	20.643	0.79	0.695	0.058
126	1.407	0.006	10.558	0.076	0.735	0.013						
127	1.364	0.006	11.444	0.085	0.791	0.016	1.041	0.016	23.756	0.877	0.773	0.059
128	1.386	0.008	11.662	0.098	0.803	0.015	1.048	0.019	23.328	0.785	0.776	0.06
129	1.42	0.005	11.53	0.119	0.81	0.015	1.138	0.026	22.565	0.834	0.846	0.064
130	1.428	0.008	10.963	0.137	0.77	0.014	1.122	0.017	21.739	0.706	0.707	0.043
131	1.417	0.006	11.65	0.163	0.77	0.017	1.094	0.028	21.295	0.895	0.982	0.083
132	1.404	0.009	11.671	0.1	0.823	0.019	1.106	0.032	21.741	0.828	0.75	0.08
133	1.451	0.004	11.153	0.105	0.756	0.013	1.121	0.018	21.617	0.404	0.954	0.058
134					0.758	0.014	1.094	0.017	20.703	0.427	0.678	0.042
135	1.386	0.012	11.964	0.082	0.808	0.02	1.091	0.044	23.895	1.452	0.674	0.085
136	1.444	0.01	11.529	0.111	0.781	0.018	1.109	0.024	20.948	0.725	0.912	0.079
137	1.44	0.007	11.148	0.09	0.803	0.015	1.106	0.016	22.223	0.746	0.83	0.056
138	1.475	0.01	12.315	0.12	0.794	0.018	1.148	0.034	27.583	2.168	0.68	0.068
139	1.361	0.006	11.63	0.148	0.803	0.016	1.01	0.016	21.131	0.44	0.713	0.049
140	1.41	0.006	10.293	0.095	0.7	0.014	1.118	0.018	20.566	0.46	0.691	0.043
141	1.348	0.003	10.464	0.13	0.751	0.013	1.051	0.012	20.939	0.368	0.659	0.034
142					0.809	0.018						
143	1.459	0.007	10.53	0.119	0.728	0.01	1.115	0.016	20.075	0.474	0.661	0.035
144	1.479	0.009	10.57	0.145	0.743	0.014	1.129	0.022	22.003	0.623	0.773	0.068
145	1.47	0.007	10.797	0.169	0.774	0.016	1.171	0.028	21.535	0.816	0.715	0.067
146	1.46	0.006	8.646	0.195	0.59	0.016	1.124	0.037	20.934	0.678	0.727	0.073
147	1.491	0.007	10.701	0.097	0.789	0.014						
148					0.718	0.015						
149	1.488	0.007	10.847	0.102	0.824	0.02						
150	1.462	0.006	10.937	0.084	0.747	0.015						
151					0.768	0.014	0.987	0.03	19.496	2.513	0.877	0.133
152	1.437	0.008	11.164	0.102	0.786	0.015	1.016	0.085	22.222	2.615	0.709	0.142
154	1.358	0.028	12.435	0.55	0.673	0.041						
155	1.494	0.007	10.753	0.157	0.777	0.012	1.089	0.044	25.784	1.371	0.762	0.078
156	1.347	0.007	10.802	0.123	0.798	0.017	0.994	0.042	26.527	1.077	0.896	0.142
157	1.444	0.01	11.865	0.134	0.809	0.018	1.091	0.039	24.516	2.36	1.005	0.137
158	1.439	0.007	11.156	0.108	0.815	0.019	1.089	0.029	22	0.919	0.825	0.091
159	1.422	0.008	11.408	0.093	0.785	0.014	1.074	0.028	23.952	0.756	0.71	0.06
160	1.432	0.004	11.425	0.187	0.818	0.018	1.03	0.027	23.326	0.857	0.738	0.067
161	1.468	0.005	11.791	0.142	0.782	0.02	1.063	0.038	21.8	1.271	0.786	0.093
162	1.481	0.011	10.672	0.103	0.8	0.017	1.113	0.03	23.546	0.721	0.859	0.075
163	1.42	0.007	11.586	0.075	0.801	0.015	1.036	0.018	24.439	0.627	0.887	0.061
164	1.433	0.009	11.604	0.102	0.821	0.021	1.02	0.026	27.194	1.211	0.908	0.103
165	1.48	0.006	11.501	0.08	0.812	0.019	1.087	0.033	23.281	0.797	0.942	0.085
166	1.436	0.003	11.247	0.08	0.779	0.015					0.898	0.074
167	1.386	0.01	11.209	0.107	0.79	0.018	1.083	0.018	24.593	0.645	0.724	0.062
168	1.443	0.007	11.52	0.11	0.784	0.017	1.087	0.023	22.241	0.86	0.694	0.063
169	1.479	0.007	11.117	0.109	0.782	0.016	1.122	0.027	22.291	0.739	0.697	0.056
170	1.385	0.007	10.487	0.087	0.704	0.013	1.061	0.011	21.028	0.465	0.663	0.041
171	1.409	0.007	10.662	0.071	0.741	0.016	1.087	0.014	22.71	0.606	0.644	0.047
172	1.487	0.006	9.527	0.136	0.643	0.013	1.202	0.016	17.295	0.401	0.618	0.031

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173	1.536	0.004	7.348	0.1	0.492	0.009	1.345	0.01	12.38	0.148	0.406	0.015
174					0.15	0.005						
177	1.15	0.002	1.838	0.028	-0.739	0.006	1.137	0.003	2.106	0.021	-0.688	0.006

Table S2. Average ^{15}N relaxation rates and reduced spectral density values of secondary structure elements of cdM2-1 in absence and presence of RNA. [cdM2-1] = 350 µM, [RNA] = 115 µM, 25 °C, and 14.1 T (^1H frequency of 600 MHz).

	Protein Region	R_1 [s^{-1}]	R_2 [s^{-1}]	R_2/R_1 [s^{-1}]	hetNOE	$J(0.87\omega_H)$ [ps]	$J(\omega_N)$ [ps]	$J(0)$ [ns]
cdM2-1	Helical region	1.42±0.05	11.3±1.1	8.0±0.8	0.76±0.05	5.2±1.0	258±10	3.0±0.3
	α1	1.44±0.03	11.0±1.0	7.9±0.9	0.78±0.04	5.0±0.8	262±6	3.0±0.4
	loop 1	1.42±0.08	13.4±2.8	9.5±1.8	0.73±0.04	6.0±0.8	256±16	3.6±0.8
	α2	1.41±0.03	11.2±0.6	7.9±0.3	0.76±0.04	5.1±0.9	258±6	3.0±0.2
	loop 2	1.31±0.01	9.4±0.1	7.1±0.1	0.72±0.02	5.8±0.4	237±2	2.44±0.03
	α3	1.37±0.05	11.5±0.2	8.4±0.3	0.75±0.02	5.3±0.2	249±10	3.03±0.05
	loop 3	1.34±0.04	10.5±0.3	7.8±0.4	0.69±0.06	6.5±1.1	242±9	2.76±0.08
	α4	1.41±0.03	11.4±0.5	8.1±0.4	0.77±0.04	4.9±0.8	257±6	3.0±0.1
	loop 4	1.35±0.01	10.5±0.1	7.8±0.1	0.78±0.04	5.2±0.3	245±1	2.75±0.04
	α5	1.47±0.01	10.4±0.8	7.1±0.5	0.74±0.07	5.9±1.7	267±5	2.7±0.2
	loop 5	1.40±0.05	11.8±0.9	8.5±1.0	0.73±0.08	5.9±1.5	253±13	3.1±0.2
	α6	1.44±0.04	11.2±0.4	7.8±0.3	0.79±0.03	4.7±0.6	262±7	2.9±0.1
cdM2-1/RNA	Helical region	1.09±0.05	22.2±2.1	20.4±2.2	0.76±0.10	4.1±1.6	198±10	6.1±0.5
	α1	1.15±0.06	21.2±2.5	18.5±2.3	0.80±0.07	3.6±1.4	210±10	5.8±0.7
	loop 1	1.15±0.02	23.4±3.5	20.4±3.4	0.72±0.05	4.9±0.9	207±4	6.4±1.0
	α2	1.08±0.03	22.9±0.9	21.3±0.6	0.72±0.15	4.9±1.1	195±7	6.3±0.2
	loop 2	1.04±0.02	18.1±0.5	17.4±0.6	0.64±0.05	5.8±0.8	185±4	4.9±0.1
	α3	1.08±0.06	21.7±0.9	20.2±1.3	0.77±0.06	3.8±1.0	196±10	5.9±0.3
	loop 3	1.05±0.02	19.8±0.2	18.9±0.2	0.61±0.11	6.4±1.8	187±5	5.4±0.1
	α4	1.09±0.04	22.3±1.8	20.4±1.6	0.77±0.10	3.9±1.8	199±8	6.1±0.5
	loop 4	1.05±0.01	20.9±0.4	19.9±0.4	0.66±0.03	5.6±0.5	188±2	5.7±0.1
	α5	1.11±0.07	20.8±1.0	18.8±0.7	0.75±0.08	4.3±1.5	200±11	5.7±0.3
	loop 5	1.01±0.08	22.2±2.6	21.9±3.2	0.71±0.14	4.6±2.3	183±16	6.1±0.7
	α6	1.07±0.03	23.7±1.7	22.2±2.1	0.80±0.11	3.4±1.8	195±6	6.5±0.5

Table S3. Extended model-free parameters for the RNA-free cdM2-1 calculated from Lipari-Szabo formalism by using TENSOR2 program (1). [cdM2-1] = 350 µM, 25 °C, and 14.1 T (^1H frequency of 600 MHz).

Residue	Model	χ^2	S^2	$\pm S^2$	τ_e	$\pm\tau_e$	R_{ex}	$\pm R_{ex}$	S_1^2	$\pm S_1^2$
59	4	0	0.2098	0.01	7.658×10^{-10}	6.1701×10^{-12}	1.6252	0.3463	1	0
60	5	0	0.0359	0.0218	8.0663×10^{-10}	1.3369×10^{-11}	0	0	0.7228	0.0087
61	5	0	0.102	0.0373	7.3078×10^{-10}	2.4301×10^{-11}	0	0	0.791	0.0169
62	5	0	0.1127	0.0445	8.2225×10^{-10}	2.9419×10^{-11}	0	0	0.7334	0.02
63	5	0	0.1175	0.0397	8.8646×10^{-10}	2.7558×10^{-11}	0	0	0.7288	0.0161
64	5	0	0.1252	0.0282	9.1484×10^{-10}	1.837×10^{-11}	0	0	0.7458	0.0118
65	5	0	0.1851	0.0163	9.1562×10^{-10}	1.2888×10^{-11}	0	0	0.8027	0.0087
66	5	0	0.233	0.0081	1.1118×10^{-9}	1.0021×10^{-11}	0	0	0.7759	0.0043
67	5	0	0.2692	0.0114	1.0766×10^{-9}	1.3397×10^{-11}	0	0	0.8334	0.0063

68	5	0	0.3188	0.0168	1.1932×10^{-9}	2.1148×10^{-11}	0	0	0.801	0.0098
69	5	0	0.4353	0.0206	1.1474×10^{-9}	3.0647×10^{-11}	0	0	0.8507	0.0122
70	5	0	0.4685	0.0136	1.289×10^{-9}	2.6651×10^{-11}	0	0	0.8587	0.0095
71	5	0	0.5101	0.0202	1.1731×10^{-9}	3.6049×10^{-11}	0	0	0.871	0.0128
72	5	0	0.7113	0.0116	1.113×10^{-9}	4.2957×10^{-11}	0	0	0.8902	0.0083
73	5	0	0.6755	0.0143	1.0116×10^{-9}	4.4876×10^{-11}	0	0	0.9234	0.0111
74	5	0	0.6832	0.0121	1.018×10^{-9}	4.1482×10^{-11}	0	0	0.8142	0.0078
75	5	0	0.8885	0.0119	1.4695×10^{-9}	2.829×10^{-10}	0	0	0.8423	0.0099
76	5	0	0.9409	0.0125	8.5909×10^{-10}	2.964×10^{-10}	0	0	0.8876	0.0132
77	1	0.26701	0.8932	0.0033	0	0	0	0	1	0
78	1	5.2035	0.9146	0.004	0	0	0	0	1	0
79	3	0.10012	0.9207	0.0098	0	0	0.5414	0.1878	1	0
80	1	0.55466	0.9276	0.0046	0	0	0	0	1	0
81	5	0	0.9712	0.009	1.6079×10^{-9}	2.4817×10^{-9}	0	0	0.9034	0.0082
82	4	0	0.9166	0.0051	3.7592×10^{-11}	1.0271×10^{-11}	0.4757	0.1679	1	0
83	5	0	0.9374	0.0074	1.1485×10^{-9}	2.4569×10^{-10}	0	0	0.9377	0.0063
84	3	0.71406	0.9246	0.0075	0	0	3.5325	0.1568	1	0
85	5	0	0.9526	0.0091	1.0526×10^{-9}	3.1883×10^{-10}	0	0	0.9217	0.0091
86	5	0	0.9541	0.0113	1.0071×10^{-9}	4.5211×10^{-10}	0	0	0.9189	0.0108
87	4	0	0.9062	0.0077	3.0475×10^{-11}	1.3091×10^{-11}	4.8611	0.1928	1	0
88	4	0	0.9477	0.0111	1.0354×10^{-10}	5.4563×10^{-11}	4.4945	0.2915	1	0
89	4	0	0.9302	0.0111	1.0735×10^{-10}	3.6407×10^{-11}	0.7294	0.3026	1	0
90	4	0	0.795	0.0066	4.4142×10^{-11}	4.52×10^{-12}	0.9954	0.185	1	0
92	1	0.46323	0.9273	0.011	0	0	0	0	1	0
93	2	0.12227	0.9207	0.0058	3.4487×10^{-11}	1.1912×10^{-11}	0	0	1	0
94	5	0	0.9671	0.0145	1.6755×10^{-9}	2.2565×10^{-9}	0	0	0.9143	0.0141
95	1	3.1494	0.9339	0.006	0	0	0	0	1	0
97	4	0	0.8953	0.0048	2.6385×10^{-11}	8.8336E-12	0.3549	0.1357	1	0
98	1	2.8853	0.9396	0.006	0	0	0	0	1	0
99	4	0	0.8905	0.005	2.733×10^{-11}	7.0879×10^{-12}	0.2854	0.1217	1	0
100	5	0	0.9114	0.0096	1.9725×10^{-9}	7.2873×10^{-10}	0	0	0.8281	0.0084
101	2	1.6289	0.9191	0.0046	2.611×10^{-11}	1.1177×10^{-11}	0	0	1	0
102	5	0	0.9665	0.0114	1.6126×10^{-9}	2.2961×10^{-9}	0	0	0.8884	0.0116
103	3	1.4586	0.917	0.0038	0	0	0.2892	0.1008	1	0
104	5	0	0.8805	0.0091	9.7263×10^{-10}	9.3315×10^{-11}	0	0	0.9079	0.0074
105	5	0	0.9473	0.0078	7.9123×10^{-10}	1.9085×10^{-10}	0	0	0.9224	0.0067
107	5	0	0.9026	0.0089	1.1819×10^{-9}	1.7391×10^{-10}	0	0	0.8147	0.0067
108	4	0	0.8931	0.0131	3.0719×10^{-11}	1.1647×10^{-11}	0.6765	0.3185	1	0
109	2	0.05724	0.9016	0.0049	3.3728×10^{-11}	6.8438×10^{-12}	0	0	1	0
110	4	0	0.8249	0.005	2.7826×10^{-11}	4.2359×10^{-12}	0.8013	0.1493	1	0
112	4	0	0.8913	0.0052	2.6592×10^{-11}	8.3969×10^{-12}	0.4009	0.1252	1	0
113	4	0	0.8579	0.0042	2.6816×10^{-11}	4.502×10^{-12}	0.7924	0.1001	1	0
114	4	0	0.8463	0.005	3.5662×10^{-11}	4.9792×10^{-12}	0.721	0.1064	1	0
115	4	0	0.879	0.0052	3.7679×10^{-11}	7.4201×10^{-12}	0.5029	0.1273	1	0
116	4	0	0.8866	0.0039	3.2551×10^{-11}	6.3567×10^{-12}	0.4327	0.0946	1	0
118	5	0	0.9525	0.0072	9.0964×10^{-10}	1.9956×10^{-12}	0	0	0.8567	0.0054
119	4	0	0.7706	0.0043	5.0437×10^{-11}	2.9214×10^{-12}	1.2515	0.0818	1	0
121	2	2.2223	0.8396	0.0072	3.9978×10^{-11}	6.8082×10^{-12}	0	0	1	0
122	2	2.9424	0.8584	0.0033	4.8594×10^{-11}	4.2949×10^{-12}	0	0	1	0
124	4	0	0.8796	0.0043	4.9169×10^{-11}	6.8322×10^{-12}	0.3206	0.1466	1	0
125	2	0.5618	0.8902	0.0049	4.0626×10^{-11}	7.5932×10^{-12}	0	0	1	0
126	5	0	0.9534	0.0092	6.6495×10^{-10}	1.5364×10^{-10}	0	0	0.8943	0.0097
127	3	3.0646	0.8779	0.0035	0	0	0.5121	0.1015	1	0
128	1	3.0936	0.9113	0.0042	0	0	0	0	1	0
129	1	0.9469	0.917	0.0028	0	0	0	0	1	0
130	2	0.01512	0.8947	0.0057	2.7401×10^{-11}	7.3341×10^{-12}	0	0	1	0
131	4	0	0.9	0.0056	2.8586×10^{-11}	9.4167×10^{-12}	0.4462	0.1683	1	0
132	1	0.71086	0.9189	0.0049	0	0	0	0	1	0
133	2	0.51786	0.9097	0.0035	4.3724×10^{-11}	7.5973×10^{-12}	0	0	1	0
135	4	0	0.8871	0.0084	3.1256×10^{-11}	6.7178×10^{-12}	0.7928	0.1325	1	0
136	1	5.2284	0.9288	0.0053	0	0	0	0	1	0

137	1	1.1943	0.9114	0.0035	0	0	0	0	1	0
138	3	1.8578	0.943	0.0066	0	0	0.6567	0.1424	1	0
139	3	1.0895	0.8874	0.0041	0	0	0.4314	0.1484	1	0
140	5	0	0.9278	0.0077	7.4509×10^{-10}	1.1759×10^{-10}	0	0	0.8916	0.0053
141	2	0.13083	0.8451	0.0031	2.3747×10^{-11}	4.1537×10^{-12}	0	0	1	0
143	5	0	0.9393	0.0081	8.3251×10^{-10}	1.5723×10^{-10}	0	0	0.9118	0.0063
144	5	0	0.9235	0.0099	1.2821×10^{-9}	2.2653×10^{-10}	0	0	0.9133	0.0084
145	5	0	0.9499	0.0132	1.4184×10^{-9}	7.236×10^{-10}	0	0	0.9135	0.014
146	5	0	0.7791	0.0157	1.1681×10^{-9}	8.7681×10^{-11}	0	0	0.8589	0.011
147	5	0	0.9437	0.0093	2.1837×10^{-9}	1.6845×10^{-9}	0	0	0.9096	0.007
149	6	0.27387	0.915	0.0145	8.5352×10^{-9}	2.7416×10^{-9}	0	0	0.9081	0.0058
150	2	2.3307	0.9031	0.0042	4.9879×10^{-11}	8.2221×10^{-12}	0	0	1	0
152	5	0	0.973	0.008	1.0634×10^{-9}	1.4617×10^{-9}	0	0	0.9167	0.0082
154	4	0	0.8558	0.0197	5.8574×10^{-11}	1.6668×10^{-11}	1.5625	0.5855	1	0
155	5	0	0.9204	0.011	2.1507×10^{-9}	7.2818×10^{-10}	0	0	0.912	0.0092
156	1	1.7409	0.8688	0.004	0	0	0	0	1	0
157	1	0.4883	0.9393	0.0052	0	0	0	0	1	0
158	5	0	0.9693	0.0092	5.0974×10^{-9}	3.1156×10^{-9}	0	0	0.9074	0.0064
159	2	0.03786	0.9113	0.0047	2.2808×10^{-11}	8.3209×10^{-12}	0	0	1	0
160	1	2.4286	0.9299	0.0027	0	0	0	0	1	0
161	1	3.7377	0.9486	0.003	0	0	0	0	1	0
162	5	0	0.918	0.0166	3.8136×10^{-9}	2.5011×10^{-9}	0	0	0.8967	0.0068
163	1	2.1651	0.9209	0.0037	0	0	0	0	1	0
164	1	1.3782	0.9285	0.0045	0	0	0	0	1	0
165	5	0	0.9743	0.0082	3.479×10^{-9}	3.1494×10^{-9}	0	0	0.9354	0.0056
166	5	0	0.97	0.0064	9.7756×10^{-10}	7.6211×10^{-10}	0	0	0.9211	0.0069
167	1	2.6755	0.8961	0.0049	0	0	0	0	1	0
168	2	1.2878	0.9246	0.0053	3.233×10^{-11}	1.2052×10^{-11}	0	0	1	0
169	5	0	0.9451	0.0077	1.7978×10^{-9}	1.2254×10^{-9}	0	0	0.9247	0.0074
170	5	0	0.9386	0.0077	6.3225×10^{-10}	1.2827×10^{-10}	0	0	0.8898	0.0062
171	5	0	0.9336	0.0065	1.0989×10^{-9}	1.946×10^{-10}	0	0	0.8954	0.0059
172	5	0	0.8123	0.0096	1.307×10^{-9}	8.5453×10^{-11}	0	0	0.8902	0.0078
173	5	0	0.602	0.0084	1.3618×10^{-9}	2.961×10^{-11}	0	0	0.8427	0.0057
177	5	0	0.0701	0.0035	6.977×10^{-10}	2.9685×10^{-12}	0	0	0.7035	0.0018

Table S4–S13. Structural detail of the non-covalent interactions determined from PLIP server (2) for the structural models of the cdM2-1/RNA complexes.

Table S4: Model 1

Hydrogen bonds				
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Glu71	3.84	✔	✔	ribose
Gly75	3.72	✔	✖	phosphate
Tyr83	2.00	✔	✔	phosphate
Ile84	3.82	✖	✖	ribose
Ser86	3.24	✔	✖	ribose
Thr91	3.42	✖	✔	base
Thr91	3.76	✔	✔	base
Thr91	3.76	✖	✔	base
Gln93	3.80	✖	✖	base
Gln93	3.31	✔	✔	base
Ser94	3.58	✔	✔	base
Ser94	3.76	✖	✔	base
Val97	3.99	✖	✖	base
Ser100	3.89	✔	✔	phosphate

Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Lys150	2.77	✔	✔	ribose
Lys158	3.68	✔	✔	base
Lys159	2.30	✔	✔	ribose

π-cation interactions

Residue	Distance (Å)	Protein charged?	RNA group
Lys150	5.20	✔	base
Lys158	5.72	✔	base

Salt bridges

Residue	Distance (Å)	Protein positive?	RNA group
Lys92	3.32	✔	phosphate[1]
Lys92	3.88	✔	phosphate[2]
Lys101	5.09	✔	phosphate[1]
Lys101	3.73	✔	phosphate[2]
Lys150	3.92	✔	phosphate[1]
Lys150	4.39	✔	phosphate[2]

Table S5: Model 2

Hydrogen bonds

Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Ser86	3.47	✔	✔	phosphate
Ser86	3.56	✘	✔	phosphate
Lys92	3.97	✔	✔	phosphate
Lys92	3.34	✔	✘	Ribose
Ser133	3.43	✔	✔	phosphate
Ser137	2.23	✔	✔	phosphate
Gln144	3.89	✔	✔	base
Thr145	3.01	✘	✘	base
Thr145	2.91	✔	✔	base
Leu148	2.95	✘	✘	ribose
Arg151	2.35	✘	✔	base
Lys158	3.01	✔	✔	ribose

π-cation interactions

Residue	Distance (Å)	Protein charged?	RNA group
Arg151	4.98	✔	base
Arg151	4.70	✔	base

Salt bridges

Residue	Distance (Å)	Protein positive?	RNA group
Lys92	3.64	✔	phosphate[1]
Lys92	3.39	✔	phosphate[2]
Lys143	5.45	✔	phosphate
His147	3.67	✔	phosphate
Lys150	5.05	✔	phosphate[1]
Lys150	4.11	✔	phosphate[2]
Lys158	2.50	✔	phosphate

Table S6: Model 3

		Hydrogen bonds		
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Gly75	4.07	✗	✗	base
Ser82	2.69	✗	✓	ribose
Tyr83	3.17	✓	✓	phosphate
Tyr83	3.17	✗	✓	phosphate
Ser86	3.22	✗	✓	ribose
Asn88	2.37	✓	✓	phosphate
Asn89	2.51	✓	✓	base
Ile90	3.63	✗	✗	phosphate
Lys92	3.76	✓	✓	phosphate
Thr104	3.99	✓	✓	ribose
Ser133	3.89	✓	✓	phosphate
Ser133	4.07	✗	✓	phosphate
Lys143	4.08	✓	✓	base
Gln144	2.94	✓	✓	base
His147	4.01	✗	✓	base
Arg151	3.30	✓	✓	base
Arg151	3.92	✓	✓	ribose
Arg151	3.92	✗	✓	ribose
Asp155	3.12	✓	✗	phosphate

		π-cation interactions	
Residue	Distance (Å)	Protein charged?	RNA group
Arg151	4.49	✓	base

		π-stacking	
Residue	Distance (Å)	Type	RNA group
His168	4.39	T-shaped	base

		Salt bridges	
Residue	Distance (Å)	Protein positive?	RNA group
Lys92	3.00	✓	phosphate[1]
Lys92	4.94	✓	phosphate[2]
Lys101	2.97	✓	phosphate
Arg126	5.02	✓	Phosphate[1]
Arg126	4.46	✓	Phosphate[2]
Lys143	4.67	✓	phosphate
Lys150	3.02	✓	Phosphate[1]
Lys150	5.37	✓	Phosphate[2]
Lys158	5.48	✓	phosphate

Table S7: Model 4

		Hydrogen bonds		
Residue	Distance (Å)	Protein	Side	RNA

Residue	Distance (Å)	Donor?	chain?	group
Ser86	1.96	✗	✓	base
Asn89	3.47	✓	✓	phosphate
Asn89	3.76	✓	✗	phosphate
Thr91	3.81	✓	✓	ribose
Gln93	3.72	✓	✓	phosphate
Ser100	4.05	✗	✗	phosphate
Thr104	3.42	✓	✓	phosphate
Thr145	3.59	✓	✓	phosphate
Thr160	2.99	✓	✗	base
Thr160	2.07	✗	✓	base
Asn163	2.59	✓	✓	ribose
Asn163	4.00	✗	✓	ribose

Salt bridges			
Residue	Distance (Å)	Protein positive?	RNA group
Lys150	4.52	✓	phosphate[1]
Lys150	2.52	✓	phosphate[2]

Table S8: Model 5

Hydrogen bonds				
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Tyr83	3.94	✓	✓	base
Lys92	3.19	✓	✓	ribose
Gln93	2.03	✓	✓	phosphate
Gln93	3.21	✗	✓	phosphate
Gln93	3.15	✗	✓	phosphate
Ser122	3.93	✗	✗	phosphate
Arg126	3.97	✓	✓	base
Arg126	3.10	✗	✗	phosphate
Asn129	3.66	✓	✓	ribose
Thr130	2.80	✓	✓	phosphate
Lys143	3.13	✓	✓	ribose
Gln144	3.66	✓	✓	phosphate
Lys150	346	✗	✗	phosphate
Lys150	2.38	✓	✓	phosphate
Arg151	3.61	✗	✓	ribose
Arg151	3.62	✓	✓	base
Arg151	1.65	✓	✓	ribose
Ala154	4.08	✓	✗	ribose

π-cation interactions			
Residue	Distance (Å)	Protein charged?	RNA group
Lys150	5.17	✓	base

Salt bridges			
Residue	Distance (Å)	Protein positive?	RNA group
Lys92	2.25	✓	phosphate

Lys143	4.36	✓	phosphate
His147	3.57	✓	phosphate[1]
His147	4.97	✓	phosphate[2]
Lys150	4.77	✓	phosphate[1]
Lys150	4.76	✓	phosphate[2]
Arg151	3.87	✓	phosphate[1]
Arg151	3.98	✓	phosphate[2]
Lys159	4.37	✓	phosphate

Table S9: Model 6

		Hydrogen bonds		
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Ser100	3.08	✓	✓	phosphate
Lys101	3.29	✓	✓	base
Thr104	2.08	✗	✓	ribose
Thr104	3.48	✓	✓	base
Arg126	2.97	✗	✓	ribose
Ser133	3.90	✓	✓	ribose
Ser137	2.50	✓	✓	phosphate
Asn138	3.21	✗	✗	phosphate
Asn141	3.70	✓	✓	phosphate
Lys143	2.73	✓	✓	base
His147	3.86	✗	✓	base
Arg151	2.85	✓	✓	base
Val156	2.70	✗	✗	phosphate

		π-cation interactions	
Residue	Distance (Å)	Protein charged?	RNA group
Lys101	3.41	✓	base
Lys143	2.42	✓	base

Table S10: Model 7

		Hydrogen bonds		
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Thr91	3.58	✓	✓	ribose
Ser94	3.67	✓	✓	phosphate
Arg126	2.01	✓	✓	phosphate
Arg126	2.37	✓	✓	phosphate
Arg126	2.47	✗	✓	phosphate
Thr130	3.78	✓	✓	ribose
Lys143	3.11	✗	✗	phosphate
Lys150	2.50	✓	✗	phosphate
Arg151	3.33	✓	✓	base
Asp155	3.95	✗	✗	phosphate
Lys159	3.42	✓	✓	ribose
Asn163	3.93	✓	✓	ribose

		Salt bridges	
Residue	Distance (Å)	Protein positive?	RNA group
Lys92	3.56	✓	phosphate
Lys101	5.34	✓	phosphate[1]
Lys101	2.80	✓	phosphate[2]
Lys143	4.46	✓	phosphate[1]
Lys143	5.09	✓	phosphate[2]
Lys150	4.16	✓	phosphate[1]
Lys150	4.30	✓	phosphate[2]
Lys159	4.04	✓	phosphate

Table S11: Model 8

		Hydrogen bonds		
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Tyr83	3.82	✓	✓	phosphate
Ser86	3.24	✗	✓	base
Asn88	3.46	✗	✗	ribose
Thr91	4.01	✓	✓	phosphate
Gln93	3.54	✓	✓	ribose
Ser94	3.43	✓	✓	phosphate
Ser133	3.99	✓	✓	phosphate
Ser133	3.99	✗	✓	phosphate
Asn141	3.24	✗	✓	ribose
Gln144	3.77	✗	✓	base
Lys150	2.70	✓	✓	ribose
Arg151	2.14	✓	✗	base
Arg151	3.75	✓	✓	base
Arg151	2.82	✓	✓	base
Leu152	2.85	✗	✗	base
Ala154	4.00	✗	✗	base
Asp155	2.82	✗	✗	phosphate
Val156	4.06	✗	✗	ribose
Leu157	3.23	✗	✗	phosphate
Lys158	3.21	✓	✓	base
Lys159	2.12	✓	✓	base

		π-cation interactions	
Residue	Distance (Å)	Protein charged?	RNA group
Arg151	4.54	✓	base

		Salt bridges	
Residue	Distance (Å)	Protein positive?	RNA group
Lys140	1.97	✓	phosphate
Lys143	2.56	✓	phosphate[1]
Lys143	4.25	✓	phosphate[2]
Lys150	4.94	✓	phosphate

Table S12: Model 9

		Hydrogen bonds		
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Tyr83	3.99	✓	✓	ribose
Ile90	3.50	✗	✗	ribose
Lys92	2.38	✓	✓	base
Lys92	2.21	✓	✗	base
Gln93	3.50	✗	✗	ribose
Arg126	3.97	✓	✓	ribose
Asn129	4.08	✓	✓	ribose
Thr130	2.96	✗	✓	ribose
Ser137	2.42	✓	✓	ribose
Asn141	2.54	✓	✓	phosphate
Gln144	3.07	✓	✓	Phosphate
Gln144	3.75	✗	✓	phosphate
Lys150	2.75	✓	✓	base
Arg151	3.58	✓	✓	base
Arg151	2.45	✓	✓	base
Arg151	2.24	✓	✓	phosphate
Asp155	3.25	✓	✗	base
Asp155	3.92	✓	✓	base
Asp155	3.92	✗	✓	base
Val156	2.93	✓	✗	base
Thr160	3.93	✗	✓	base

		π-cation interactions	
Residue	Distance (Å)	Protein charged?	RNA group
His147	3.63	✓	base
Lys150	2.76	✓	base[*]
Lys150	3.00	✓	base[*]

		Salt bridges	
Residue	Distance (Å)	Protein positive?	RNA group
Lys92	3.99	✓	phosphate[1]
Lys92	3.84	✓	phosphate[2]
His147	5.25	✓	phosphate
Lys150	4.56	✓	phosphate
Arg151	2.50	✓	phosphate

Table S13: Model 10

		Hydrogen bonds		
Residue	Distance (Å)	Protein Donor?	Side chain?	RNA group
Glu81	3.25	✗	✓	base
Ser82	2.42	✓	✓	phosphate
Tyr83	2.34	✓	✓	phosphate
Ile84	2.88	✗	✗	base
Gly85	2.79	✗	✗	base

Residue	Distance (Å)			RNA group
Asn88	2.38	✖	✔	ribose
Asn88	3.72	✔	✔	phosphate
Thr91	4.02	✔	✖	base
Thr91	3.82	✔	✔	base
Thr91	3.82	✖	✔	base
Lys92	3.10	✔	✖	phosphate
Arg126	3.38	✔	✔	ribose
Thr130	3.09	✔	✔	phosphate
Lys143	4.07	✔	✔	base
Gln144	3.87	✔	✔	base
Gln144	3.88	✖	✔	base
Lys150	3.87	✔	✔	base
Arg151	3.84	✔	✔	phosphate
Arg151	4.03	✔	✔	base
Ala154	3.61	✖	✖	phosphate
Lys159	2.72	✔	✔	ribose
Lys169	2.10	✔	✔	base

π-cation interactions

Residue	Distance (Å)	Protein charged?	RNA group
His147	4.36	✔	base
Lys169	2.78	✔	base

π-stacking

Residue	Distance (Å)	Type	RNA group
His147	4.42	parallel	base
His147	3.04	parallel	base*
His147	2.90	parallel	base*

Salt bridges

Residue	Distance (Å)	Protein positive?	RNA group
Lys92	5.08	✔	phosphate[1]
Lys92	4.14	✔	phosphate[2]
Lys92	5.27	✔	phosphate[3]
Lys150	2.53	✔	phosphate[1]
Lys150	4.08	✔	phosphate[2]
Lys159	5.11	✔	phosphate

Table S14. The primary sequences of 10 RNAs were generated from the Random Sequence Generator (RSG) webserver (www.molbiotools.com) setting the length of sequence equal to 40 and AU content at 80%.

RNA sequences
AUAAGUUUAUUAUUAAAUUCAAAAGUUAAAACUUUAUAUU
AAACUUUUACAUUUGUUUAUUGAAAAUUUUGAUAUUAGUU
AUCUUAUAAAAUUACUACAUUAGGUUGGUUAUUGUUAUAC
GUCUAAAAUGUAUAUCUCAUAUAUAAUGAAAUACAUACUG

13

AUUAAGCUAAUAAUAUUAUGAGUUUGUAUUGAUUAUGUUU
ACGAUUUAAAGAUGGAGUACUCACUAUUUUGAUUAUAGAU
UAUAAAACGAUAUAGAAAUUUUUUAUUAUUAUAGUUUGAA
GUAGGUUUAGUAUGUAAGUAACCACUAUACAGUUUAAACA
AAGAUUGUUAUAAUAAAUCAUGACUUUUUUAAAUUAAAUA
AGAGUUAAUAUCUUGCUAAAUUUACUAAGACAAUAUUUUU

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