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SUPPLEMENTARY MATERIAL TO

Diversifying the chloroquinoline scaffold against SARS-CoV-2 main protease: Virtual screening approach using cross-docking, SiteMap analysis and molecular dynamics simulation

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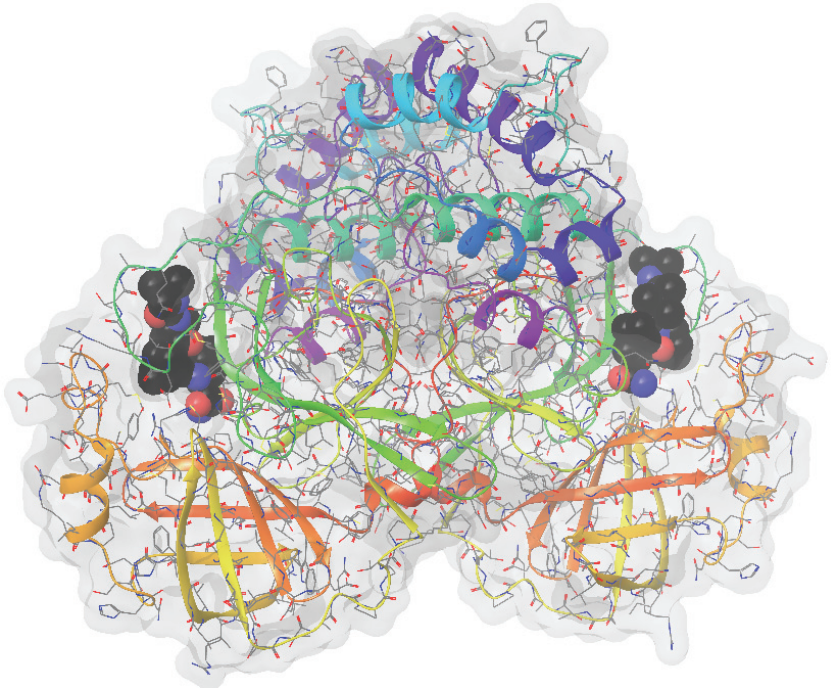

Fig. S-1. Crystal structure of [SARS-CoV-2/M^{pro}] complex (PDB ID: 7BRP).

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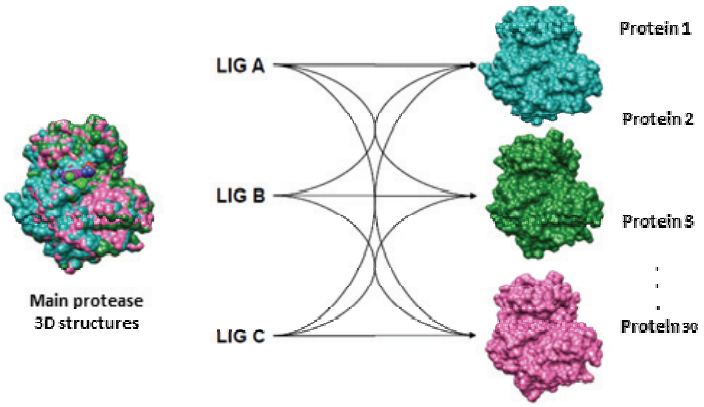

Fig. S-2. Cross-docking schematic approach.

	6LZE	6WCO	6WTK	6XBG	6XHM	7BQY	7BRP	7BUY	7K40	6M2N	6XA4	6XR3	6LU7	6M0K	6W63	6W79	6WNP	6WTJ	6WTT	6XBH	6XBI	6XFN	6Y2F	6Y2G	6ZRU	7C8R	7C8T	7COM	7D3I	7JYC
6LZE	**2.30**	4.59	2.30	3.82	3.06	4.22	2.54	10.51	3.71	5.20	8.25	5.50	5.73	4.99	5.16	6.94	4.76	7.29	9.93	9.02	4.97	6.50	4.03	4.09	3.59	3.54	9.79	7.61	4.18	4.35
6WCO	5.64	**5.58**	5.89	5.87	5.72	2.04	2.23	4.91	3.66	4.66	8.37	5.66	4.23	8.17	6.94	9.08	4.53	4.59	4.12	4.73	5.79	13.35	4.73	3.10	4.15	4.11	4.64	5.55	3.86	10.51
6WTK	6.78	5.39	**5.08**	4.52	4.51	4.98	2.26	4.64	5.15	2.68	8.16	5.37	3.31	6.50	10.58	6.88	4.26	6.13	4.00	5.62	5.78	8.15	4.52	6.41	4.31	3.47	3.83	8.82	5.43	5.27
6XBG	4.77	6.06	4.70	**4.38**	9.27	4.80	4.82	4.77	4.28	4.26	8.37	5.67	4.07	6.94	1.27	8.60	4.93	9.37	5.45	5.78	8.03	7.36	5.71	5.26	8.33	5.08	4.53	8.88	4.79	8.05
6XHM	6.88	8.51	3.73	4.08	**3.50**	4.26	2.13	5.70	4.11	5.18	8.30	5.55	5.00	7.41	1.43	8.59	10.69	7.53	5.71	5.50	5.83	4.93	5.70	7.66	3.63	5.22	4.55	5.45	4.07	7.17
7BQY	6.54	8.42	8.76	5.04	8.13	**5.42**	1.79	7.15	5.26	6.76	6.68	9.61	8.20	3.48	5.27	8.26	4.05	6.23	5.80	5.79	4.25	9.67	3.60	4.40	5.14	4.92	5.66	2.40	4.47	5.63
7BRP	5.98	8.22	5.80	5.21	8.66	6.71	**1.65**	7.45	3.53	7.28	7.03	5.17	8.15	5.09	5.01	5.86	5.33	5.62	2.44	5.66	1.36	6.35	2.31	3.58	3.68	5.22	5.39	2.58	10.27	10.99
7BUY	7.51	7.14	3.13	6.59	3.81	5.37	1.42	**5.86**	8.76	4.93	7.39	5.68	8.19	5.85	5.25	8.31	6.61	5.76	8.09	6.31	8.31	5.34	8.32	5.76	2.86	5.13	5.40	10.75	5.59	5.63
7K40	6.14	8.24	5.75	5.32	8.63	6.82	1.65	5.14	**2.35**	5.85	4.25	4.94	8.14	8.13	6.80	7.63	4.15	2.25	8.16	6.34	8.27	5.05	5.39	5.48	3.03	5.16	2.82	4.49	5.17	1.78
6M2N	5.89	2.91	6.68	5.63	5.99	4.83	1.70	6.99	2.26	**6.80**	3.68	5.52	8.24	5.58	6.93	1.12	2.49	4.63	3.73	4.71	3.94	5.18	9.82	3.53	2.91	4.07	6.61	5.67	3.74	1.51
6XA4	5.55	7.05	2.49	6.02	6.06	2.29	3.53	4.06	2.52	5.58	**3.64**	6.05	5.31	5.40	5.13	7.56	6.68	1.53	5.27	5.21	5.78	5.12	5.22	4.93	3.00	3.85	7.64	4.50	5.03	1.99
6XR3	5.25	8.91	5.10	5.45	5.10	5.42	4.48	5.99	2.27	7.34	11.67	**4.68**	3.64	2.44	2.86	1.08	7.02	9.95	6.04	7.21	6.51	6.66	5.13	5.77	2.97	5.16	3.22	3.92	3.20	1.57
6LU7	7.16	7.09	8.73	9.99	8.50	9.99	2.98	8.38	2.32	7.57	10.52	3.94	**4.95**	2.36	5.48	1.14	8.58	3.40	4.30	0.97	7.46	4.94	6.18	3.23	5.45	4.78	3.52	3.75	4.82	1.59
6M0K	2.99	5.46	7.57	1.60	3.88	4.28	3.07	6.06	7.75	7.22	6.87	9.30	5.82	**6.53**	1.03	5.44	8.66	3.57	3.99	11.58	7.31	8.54	4.53	3.54	6.97	6.45	3.16	5.31	8.52	5.10
6W63	1.59	6.14	6.02	7.06	5.91	6.06	1.67	9.97	9.15	7.59	4.56	9.19	5.91	6.31	**2.33**	8.64	8.56	3.43	5.38	6.87	6.22	2.86	5.29	3.16	5.13	9.15	3.49	4.02	8.47	4.11
6W79	1.37	6.02	5.94	7.01	5.84	5.97	2.59	9.26	9.29	7.49	5.27	4.41	5.16	6.86	8.38	**3.39**	8.66	3.56	5.57	4.44	1.54	3.36	4.69	3.52	3.17	4.53	3.40	5.41	2.74	8.58
6WNP	5.61	7.82	6.00	5.05	8.63	6.33	2.00	6.04	5.03	8.93	5.26	4.81	6.15	8.42	9.99	4.73	**1.66**	3.43	5.20	6.94	9.90	7.57	9.12	3.40	10.29	9.91	8.41	9.78	2.90	3.67
6WTJ	7.07	7.97	4.39	6.53	4.18	5.23	3.50	4.99	9.98	5.44	3.29	4.86	5.27	2.19	6.80	7.48	9.98	**3.47**	5.59	7.18	5.20	5.95	6.30	4.27	5.57	6.60	4.30	4.54	2.80	3.91
6WTT	7.10	8.64	4.11	6.19	4.05	3.96	3.63	4.44	4.31	6.02	3.12	4.41	5.46	8.63	7.07	5.09	6.09	4.18	**5.43**	7.56	5.22	4.72	8.61	4.00	6.52	3.25	3.95	5.79	2.95	5.15
6XBH	8.18	5.71	4.89	4.56	7.43	7.26	3.02	4.38	9.85	6.02	5.13	5.40	1.34	8.60	3.68	8.51	5.51	4.63	7.78	**1.43**	5.19	7.23	8.57	4.22	2.78	6.60	4.77	3.29	2.79	5.52
6XBI	9.40	4.70	4.31	7.59	5.99	4.30	4.10	5.89	6.60	8.69	5.41	3.06	6.21	8.75	4.07	4.05	6.44	2.97	5.59	5.87	**5.20**	6.15	8.67	3.12	4.56	4.31	3.10	3.50	3.78	5.46
6XFN	7.93	7.80	7.75	6.34	7.23	8.09	4.86	5.97	6.01	8.76	5.33	5.78	8.26	8.57	3.48	4.41	3.02	5.20	10.22	5.97	5.21	**8.69**	4.69	5.53	2.84	8.93	3.01	3.24	6.58	5.57
6Y2F	3.13	8.30	9.03	9.45	9.07	8.99	1.66	5.42	5.98	5.78	5.72	5.87	2.08	8.61	4.07	3.82	4.87	8.04	2.63	6.12	5.59	8.85	**5.39**	5.45	2.74	8.87	3.40	3.44	10.39	6.21
6Y2G	3.19	8.26	9.10	9.58	9.18	9.02	1.79	7.65	5.85	3.64	5.92	5.91	5.95	7.45	3.86	4.39	8.07	8.11	2.01	5.89	5.33	8.53	5.48	**5.55**	6.45	8.02	6.00	3.44	8.47	8.71
6ZRU	6.12	8.26	5.79	5.30	8.61	6.79	1.57	7.88	6.20	5.97	8.97	7.20	9.26	5.53	3.54	4.21	5.59	5.70	7.80	6.30	5.77	8.89	9.18	8.01	**6.46**	9.94	6.12	6.35	6.59	4.49
7C8R	8.89	9.53	10.23	6.59	7.44	6.10	2.23	4.09	4.50	7.28	5.58	10.81	4.81	4.45	9.44	7.46	5.73	5.80	4.79	7.43	5.85	8.79	9.05	4.56	8.67	**5.08**	4.62	6.42	6.63	7.76
7C8T	6.29	8.53	5.97	4.94	6.16	3.42	4.09	4.29	3.62	7.38	4.65	4.69	6.23	5.47	7.03	3.98	5.06	9.87	1.76	7.32	3.82	7.14	9.27	4.49	4.30	5.04	**5.65**	4.50	10.12	8.46
7COM	5.88	7.98	5.85	5.19	8.65	6.62	1.82	4.01	5.93	11.21	6.50	8.01	3.98	5.54	7.77	4.94	5.17	7.75	8.43	4.43	7.89	7.23	9.02	7.55	3.27	6.41	5.11	**7.09**	2.78	8.07
7D3I	6.74	7.73	4.51	7.46	7.20	6.60	2.91	4.23	8.34	5.41	4.35	5.74	7.41	7.73	8.85	7.43	5.17	4.50	6.25	4.54	5.20	7.06	9.11	4.46	9.26	4.95	5.75	6.24	**2.64**	4.05
7JYC	10.38	9.33	5.97	6.99	10.79	6.58	3.38	4.24	5.21	7.53	6.81	4.29	7.68	6.06	7.43	7.93	8.20	6.23	4.77	6.49	4.66	2.51	7.54	7.30	5.47	6.33	5.02	9.02	1.77	**4.04**
RMSD avrge	**5.94**	**7.21**	**5.85**	**5.98**	**6.71**	**5.76**	**2.70**	**6.01**	**5.46**	**6.48**	**6.30**	**5.90**	**5.80**	**6.27**	**5.56**	**5.90**	**6.02**	**5.49**	**5.54**	**5.97**	**5.71**	**6.76**	**6.51**	**4.84**	**4.92**	**5.80**	**4.90**	**5.53**	**5.18**	**5.50**

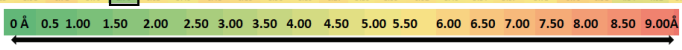

Fig. S-3. RMSD summary results of the cross-docking calculation.

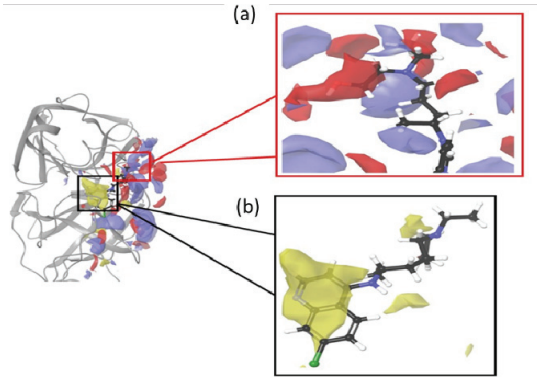

Fig. S-4. Focus on the SiteMap analysis of the M^{pro}-HCQ complex: a) hydrophilic region and b) hydrophobic region.

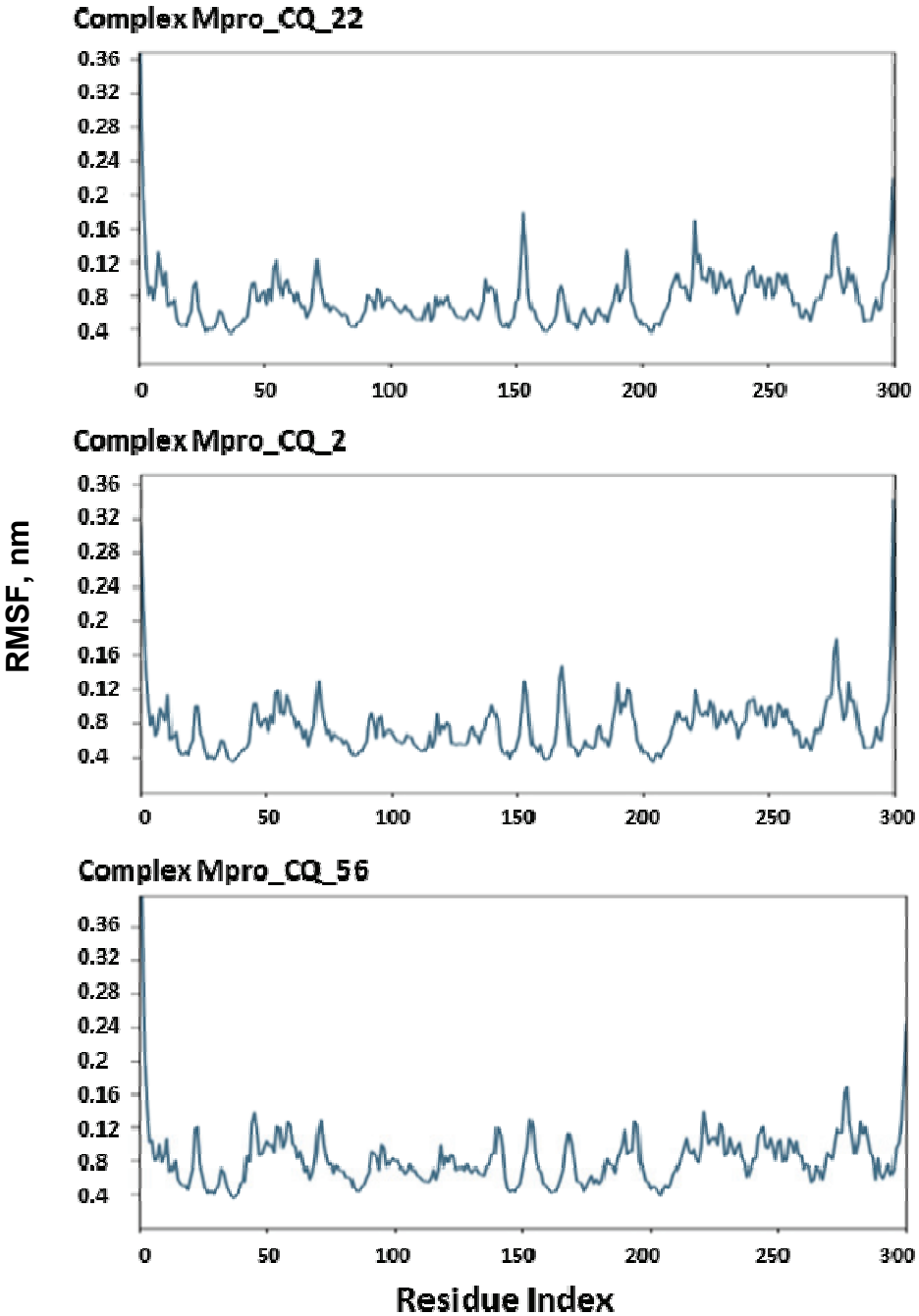

Fig. S-5. RMSF of the M^{pro} enzyme in complex with CQ_22, CQ_2 and CQ_56 during the 100 ns period of the MD simulation.

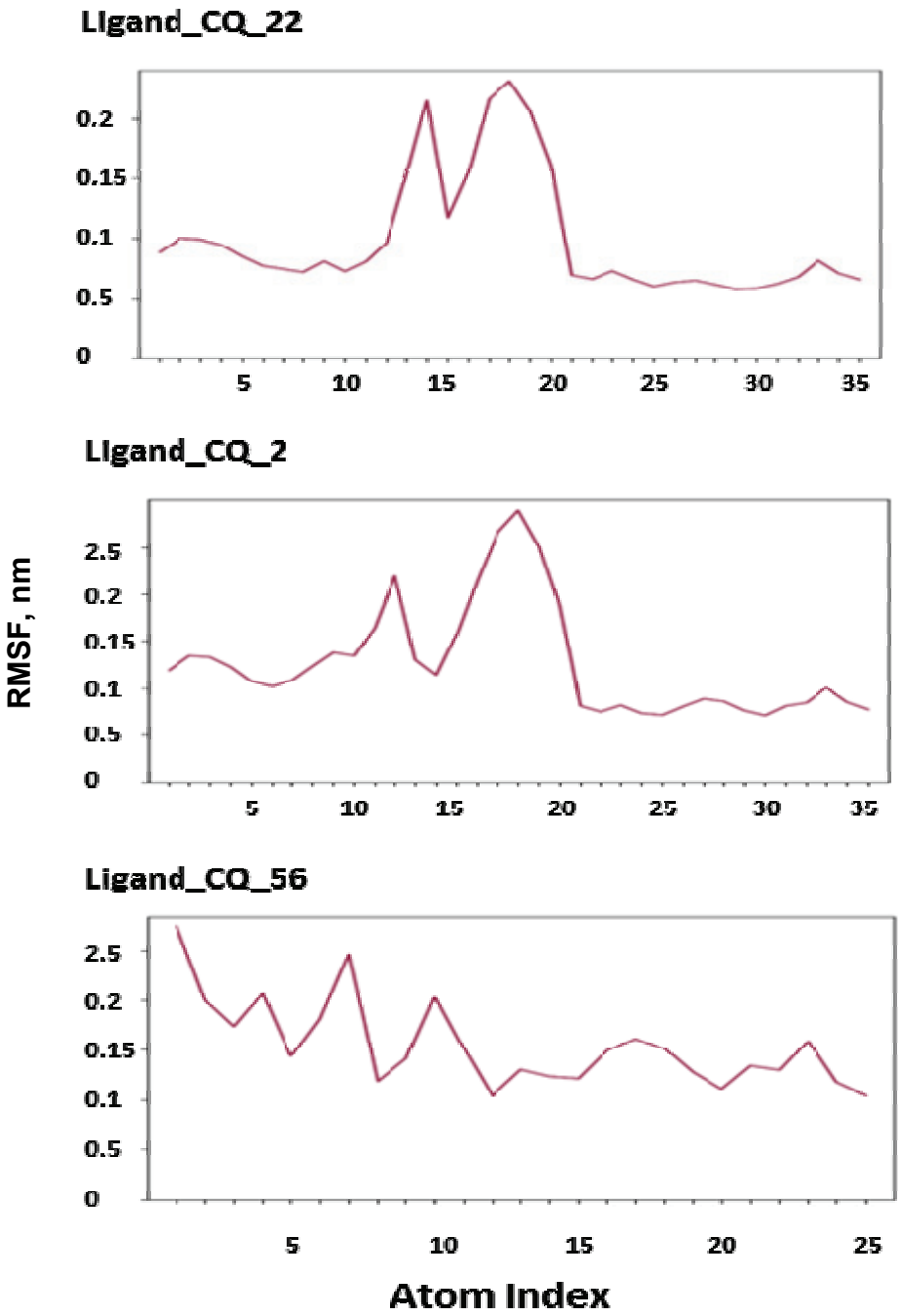

Fig. S-6. Root mean square fluctuation: During the 100 ns timeframe of the MD simulation, the RMSF of the complexed ligands CQ_22, CQ_2 and CQ_56.

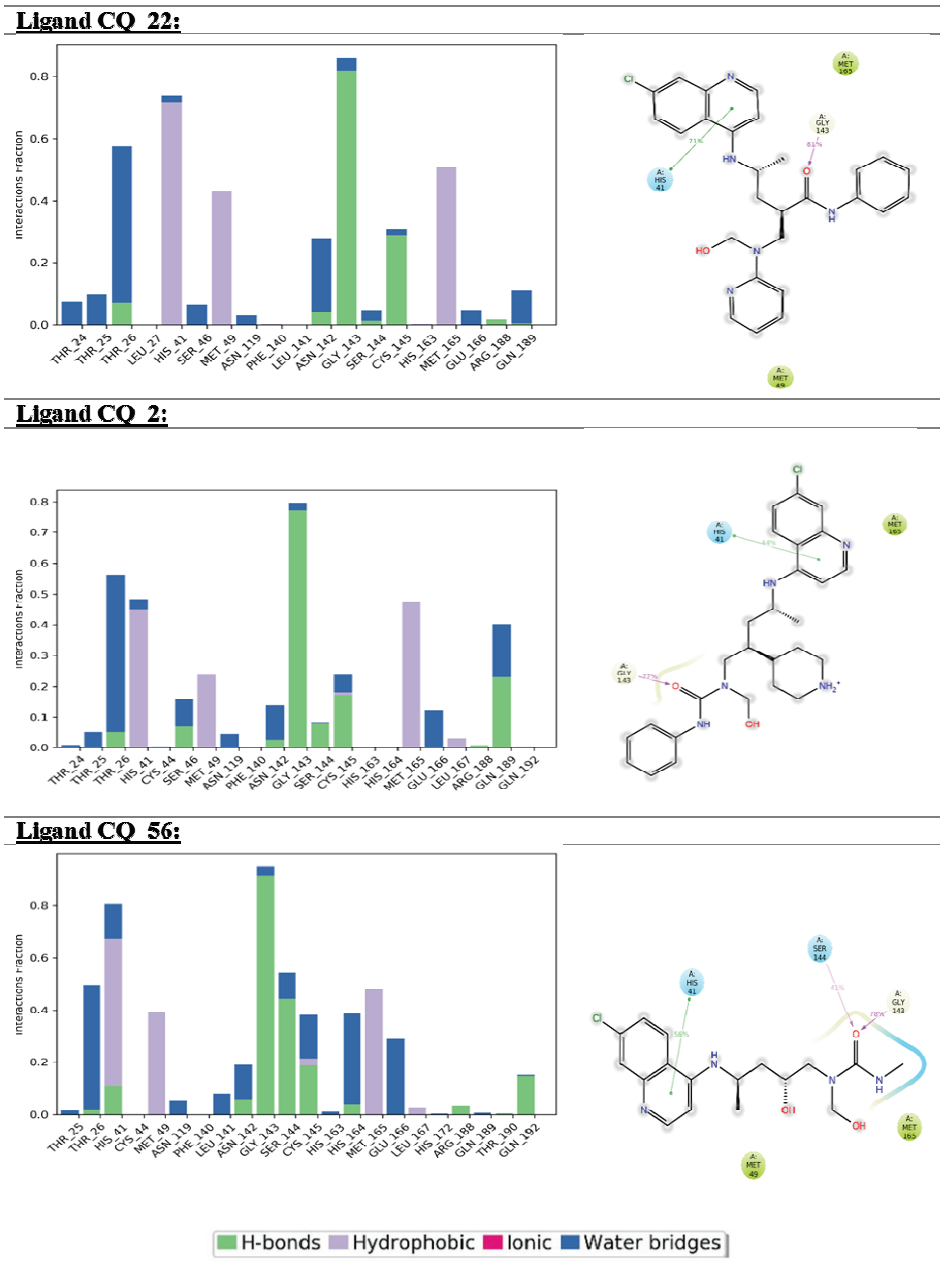

Fig. S-7. Protein–ligand contact during 100 ns MD simulation timescale.

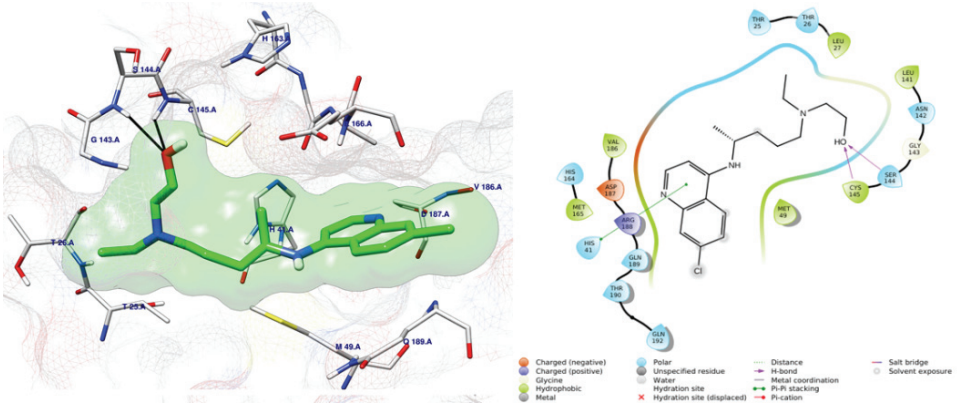

Fig. S-8. Binding disposition of HCQ after docking calculations in the active site of M^{pro}; HCQ in green sticks. H-bonds are shown as black lines. The 2D interaction diagram is shown i in the lower panel.