Dataset S1 Summary of the ligand-bound entries.

species	protein				ligand				comments																													dimer		
										PC1					C-loop conformation								distance 2-214	PC1					C-loop conformation								distance 2-214	PC1 Domain III	PC2 Domain III	distance between two 285 Cα's
	PDB ID	mutation	residues added to N-term	missing N-terminal residues#	name in PDB	name by authors	peptide or peptide mimic$	Ki, IC_{50}*, EC_{50}^{+} (μM)		C-loop	E-loop	H-loop	Linker	Domain III	main-chain HB within 138-144	HB 138-172&	HB 139-126&	HB 140-1&	HB 141-118&	HB 143-28&	distance 165Cα-140Cβ	distance 165Cα-141Cβ		C-loop	E-loop	H-loop	Linker	Domain III	main-chain HB within 138-144	HB 138-172&	HB 139-126&	HB 140-1&	HB 141-118&	HB 143-28&	distance 165Cα-140Cβ	distance 165Cα-141Cβ				
SARS-CoV	1uk4			SG of A	5-mer peptide of inhibitor	hexa-peptidyl CMK inhibitor	P	2000*	Cbz-VNSTLQ-CMK becomes NSTLQ-C-C145 in the complex. Cbz-V is not modeled.	0.554	-0.087	-0.725	1.827	13.677		1	1	1	1	1	8.311	12.537		-5.743	-0.861	-0.055	-0.542	3.948	141O-143N	0	0	0	0	0	13.049	7.664		11.47	12.946	8.407
	1wof		GPLGS	G(-5) of A, GPL of B	I12	N1	P	10.7		0.642	1.136	-1.080	0.003	10.680	141O-144N	1	1	1	1	1	7.590	11.529	8.547	0.123	-0.472	-0.523	-1.754	2.011	141O-144N	1	1	0	1	1	7.684	11.473	6.905	13.014	6.032	7.907
	1z1j_A	C145A			C-term of another chain A		P		Chain A binds a symmetrically related A chain (301-306) while chain B is in free state. C145A makes the protein inactive.	1.129	0.756	-0.317	2.256	6.628	141O-144N	0	1	1	1	1	7.215	10.533	8.134															8.53	1.861	5.767
	2a5i				AZP	Aza-peptide epoxide (APE)	P	18		0.310	1.442	-1.495	0.703	2.678	141O-144N	1	1	1	1	1	8.069	11.768	7.296															-0.001	1.775	6.885
	2a5k		A	A of A,B	AZP	Aza-peptide epoxide (APE)	P			0.313	0.878	-0.808	-2.591	4.083	141O-144N	1	1	0	1	1	7.886	11.504	7.595	0.284	0.461	-0.885	0.783	4.706	141O-144N	1	1	0	1	1	7.885	11.684	7.707	0.64	6.765	8.839
	2alv			S	CY6	4	P	70*	Mutations of T304V,F305V,Q306V.	0.371	0.496	-1.282	0.718	0.009	141O-144N	1	1	0	1	1	7.708	11.899	7.805															0	3.262	6.705
	2amd		GPLGS	G(-5) of A, GPL of B	9IN	N9	P	6.7		0.617	1.326	-1.212	-0.300	12.519	141O-144N	1	1	1	1	1	7.556	11.471	9.548	0.257	-0.738	-0.832	-1.998	2.543	141O-144N	1	1	0	1	1	7.612	11.370	7.026	13.631	7.25	8.085
	2amq		GPLGS	GPLGSSG of A, GPLGS of B	PRD_002214	N3	P	9		0.654	1.128	-0.986	-0.029	10.525	141O-144N	1	1	1	1	1	7.871	11.795		0.306	0.182	-0.609	-0.682	2.501	141O-144N	1	1	0	1	1	7.590	11.427	7.184	12.321	6.807	7.979
	2d2d		GPLGS	GPLGSSG of A, GPLGS of B	ENB	I2	P			0.598	1.191	-0.232	0.765	14.349	141O-144N	1	1	1	1	1	8.165	12.139		0.174	0.766	0.200	0.084	-0.058	141O-144N	1	1	0	1	1	8.096	11.699	7.125	13.812	5.508	8.180
	2gtb		A	AS	AZP	Aza-peptide epoxide (APE)	P			0.467	0.317	-0.665	-0.653	4.546	141O-144N	1	1	0	1	1	8.031	11.725	7.793															0.001	11.181	7.694
	2gx4				NOL	TG-0205221	P	0.053		0.756	1.011	-0.422	1.167	3.838	141O-144N	1	1	1	1	1	7.470	11.118	7.296															0.002	3.231	8.018
	2gz7				D3F	3		0.3*	D3F makes H41 flip out, making distance to C145 Sg more than 9A.	0.439	0.715	-0.404	1.613	4.980	141O-144N	1	1	1	1	1	7.935	11.560	8.381															0	5.83	7.754
	2gz8				F3F	15		3*		0.591	0.484	-0.357	1.504	4.664	141O-144N	1	1	1	1	1	7.734	11.447	7.57															0	5.363	7.841
	2hob				PRD_002214	N3	P	1.9		0.743	1.143	-0.273	0.544	5.270	141O-144N	1	1	1	1	1	7.579	11.346	7.501															0.002	3.636	8.032
	2op9		A	A of B	WR1	WRR 183	P	2.2	Non-covalent (distance between WR1 and C145 is 2.8Å) in chain A; covalent (1.8Å) in chain B. Both epoxide is eliminated. C-terminal 5 residues do not exist.	0.244	-0.056	0.401	1.264	-0.522	141O-144N	1	1	0	1	1	7.619	11.651	6.911	0.554	0.232		2.344	11.283	141O-144N	1	1	1	1	1	7.845	11.832	8.493	-10.339	7.748	8.094
	2q6g	H41A			polypeptide chain	N-terminal substrate	P		Chain A has the intact 11 residues of the substrate; chain B has only N-terminal 8 residues. H41A makes the protein inactive.	0.390	0.777	-0.304	0.046	11.445	141O-144N	1	1	0	1	1	7.287	11.001	8.83	-1.018	-0.389	-0.248	-1.348	0.339		1	1	0	1	1	7.319	10.873	7.364	14.75	8.742	8.360
	2qiq	S1A			CYV	3	P	80*	Non-covalent (distance between CYV and C145 is 2.5Å), while the bond length of C5-C6 of CYV is 1.5 A of a reacted single bond. C-terminal 5 residues are note modeled.	0.312	0.580	-1.004	1.112	4.454	141O-144N	1	1	0	1	1	7.571	11.692	8.587															0	7.748	8.195
	2v6n				XP1	XP-59		1.38	XP-59 becomes XP1 upon binding.	0.606	0.973	-0.866	1.049	7.478	141O-144N	1	1	1	1	1	7.553	11.364	7.658															0	6.027	7.998
	2vj1	S1 del	S1 del	S1 del	BEZ	XP-27			XP-27 becomes BEZ upon binding. BEZ of chain A binds to M49 and M165A, BEZ of chain B binds to C145 and E166B. After 303, 6 His are added. Deletion of S1 imapirs dimerization.	-0.426	-0.526	-0.131	2.364	13.997	141O-143N	1	1	0	1	1	7.900	12.173	7.607	-7.382	-0.803	0.179	0.763	-1.926	141O-144N	0	0	0	0	0	13.360	8.212	8.408	13.364	10.982	8.279
	2z3c				PRD_000250	1	P	0.25	Soaking. Phthalhydrazide group of 1 is eliminated to make PRD_000250 upon binding.	0.691	0.905	-0.677	0.682	5.671	141O-144N	1	1	1	1	1	7.388	11.211	7.165															-0.001	4.515	7.413
	2z3d				PRD_000235	2	P		Phthalhydrazide group of 2 is eliminated to make PRD_000250 upon binding.	0.559	1.002	-1.247	1.107	6.870	141O-144N	1	1	1	1	1	7.654	11.477	7.497															0	6.507	7.514
	2z3e				PRD_000250	1	P	0.25	Co-crystallized. Phthalhydrazide group of 1 is eliminated to make PRD_000250 upon binding.	0.540	0.996	-0.362	1.072	5.326		1	1	1	1	1	7.598	11.558	7.565															0.001	4.673	7.284
	2z94				TLD+Zn	TDT		1.4	C145 binds to Zn of TDT+Zn.	0.554	0.752	-0.410	1.940	6.344	141O-144N	1	1	1	1	1	7.711	11.469	7.674															0	5.208	7.949
	2z9g				BNZ+Hg	PMA		0.7	C145 is far from BNZ, but Hg binds to C44 and Y54.PMA becomes benzen upon binding.	0.603	0.329	-1.043	1.482	5.224	141O-144N	1	1	1	1	1	7.627	11.394	7.589															0	4.793	7.912
	2z9j				DTZ	EPDTC		1	C145 binds to Zn of DTZ. EPDTC becomes DTZ upon binding.	-0.008	-0.004	-0.282	1.391	-1.589	141O-144N	1	0	1	1	1	7.429	11.523	6.811	0.491	0.382	-0.992	2.232	12.257	141O-144N	1	1	1	1	1	7.607	11.508	8.064	-14.666	7.814	8.272
	2z9k				DOZ	JMF1600		0.32	C145 binds to Zn of DAZ. JMF1600 becomes DOZ upon binding.	0.558	0.683	-0.835	2.374	10.733	141O-144N	1	1	1	1	1	7.687	11.475	8.038	0.306	0.399	-0.183	1.284	2.638	141O-144N	1	1	1	1	1	7.662	11.518	7.108	11.317	8.405	8.291
	2z9l				DAZ	JMF1586		0.05	C145 binds to Zn of DAZ. JMF1586 becomes DAZ upon binding.	0.526	0.463		2.162	8.985	141O-144N	1	1	1	1	1	7.595	11.472	7.51	0.508	-0.096	-0.228	0.857	-3.806	141O-144N	1	1	1	1	1	7.772	11.344	6.882	11.382	2.886	7.591
	2zu4				PRD_000568	TG-0204998	P	0.038		0.847	1.277	-0.556	0.556	1.560	141O-144N	1	1	1	1	1	7.348	11.011	7.221															-0.002	0.966	7.633
	2zu5				PRD_000569	TG-0205486	P	0.099		0.723	1.492	-0.152	0.630	5.711	141O-144N	1	1	1	1	1	7.501	11.207	7.483															0.001	3.954	8.014
	3atw	R188I			PRD_000815	35	P	0.098*	Non-covalent (distance between the ligand and C145 is 2.5Å in chain A and 2.7Å in chain B). R188I is to prevent proteolysis and increases the activity.	0.491	-0.560	0.128	-2.476	-12.038	141O-144N	1	1	1	1	1	7.348	10.864	6.405	0.605	0.007	0.287	-0.251	2.820	141O-144N	1	1	1	1	1	7.549	11.096	8.642	-7.775	-5.11	6.368
	3avz	R188I			PRD_000990	31	P	0.065*	Side-chains of Thr285 clashes each other (2.2Å between two Cβ's). R188I is to prevent proteolysis and increases the activity.	0.418	0.641	-0.323	0.382	-5.214	141O-144N	1	1	1	1	1	7.386	10.822	6.569															0.001	-7.823	5.107
	3aw0	R188I			PRD_001000	16	P	5.7*	Non-covalent (distance between the ligand and C145 is 2.4Å).R188I is to prevent proteolysis and increases the activity.	0.763	0.739	-0.875	0.604	6.195	141O-144N	1	1	1	1	1	7.530	11.190	7.79															0.001	5.429	8.050
	3d62	S1, G2 del	S1, G2 del	S1, G2 del	959	4		0.4	Br of compound 4 is replaced by Sg of C145. The Boc moiety is not modeled. C-terminal 7 residues do not exist.	1.561	-1.293	-0.870	0.073	-7.747		1	1	0	0	1	7.369	11.498																-0.001	-6.66	7.120
	3sn8				PRD_001114	Cm-FF-H	P	2.24		0.489	0.468	-1.020	1.850	2.843	141O-144N	1	1	1	1	1	7.674	11.252	7.201															0.001	3.62	7.353
	3sna				PRD_001117	Ac-NSFSQ-H	P	72.73	C-terminal 5 residues do not exist.	0.657	-0.408	-1.277	2.345	0.332	141O-144N	1	1	1	1	1	7.600	11.463	7.067															0	0.849	6.665
	3snb				PRD_001118	Ac-DSFDQ-H	P	41.24		0.565	0.608	-0.718	1.312	6.155	141O-144N	1	1	1	1	1	7.718	11.421	7.554															0.001	6.034	7.984
	3snc				PRD_000771	Ac-NSTSQ-H	P	40.98		0.531	0.217	-1.155	1.588	3.781	141O-144N	1	1	1	1	1	7.621	11.177	7.446															-0.001	4.794	7.283
	3snd				PRD_000772	Ac-ESTLQ-H	P	8.27	Cocrystalization.	0.381	0.067	-0.514	0.684	4.218	141O-144N	1	1	1	1	1	7.752	11.537	7.402	0.651	0.530	0.571	1.612	9.325	141O-144N	1	1	1	1	1	7.567	11.313	8.452	-8.31	8.024	8.418
	3sne				PRD_000772	Ac-ESTLQ-H	P	8.27	Soaking.	0.641	0.262	-0.535	0.772	5.418	141O-144N	1	1	1	1	1	7.747	11.441	7.451															0.001	5.628	8.070
	3szn				G75	SG75	P			0.617	1.412	-0.968	1.728	6.202	141O-144N	1	1	1	1	1	7.724	11.434	7.491															0	4.057	7.892
	3tit				G81	SG81	P			0.582	1.200	-0.944	1.934	5.073	141O-144N	1	1	1	1	1	7.651	11.337	7.449															0.001	4.933	7.672
	3tiu				G82	SG82	P			0.679	0.983	-0.814	1.047	4.364	141O-144N	1	1	1	1	1	7.590	11.358	7.479															0	3.789	7.726
	3tns				G83	SG83	P			0.524	1.316	-0.737	0.448	3.098	141O-144N	1	1	1	1	1	7.648	11.367	7.253															-0.001	1.863	7.078
	3tnt				G85	SG85	P			0.417	1.340	-0.042	0.668	4.651	141O-144N	1	1	1	1	1	7.815	11.596	7.475															0	3.233	7.404
	3v3m				0EN	ML188(16-(R))		1.5*		0.338	0.236	-1.572	1.814	5.557	141O-144N	1	1	1	1	1	7.706	11.234	7.418															0.001	5.151	6.974
	3vb4				PRD_000910	B4Z	P	49		0.845	-0.626	-0.723	-0.583	-6.993	141O-144N	1	1	1	1	1	7.890	11.846	6.604	0.817	0.046	0.980	0.379	7.397		1	1	1	1	1	7.729	11.677	8.018	-13.389	3.127	6.970
	3vb5				PRD_000911	C4Z	P	4.6		0.754	0.480	0.026	0.697	-2.385	141O-144N	1	1	1	1	1	7.605	11.118	6.988	0.853	0.530	0.582	1.159	10.814	141O-144N	1	1	1	1	1	7.656	11.278	8.031	-13.905	7.166	8.228
	3vb6				PRD_000912	C6Z	P	39	Cbz, T, and S of C6Z are not modeled.	0.003	-0.571	-0.281	0.649	-4.244	141O-144N	1	1	1	1	1	7.483	11.460	7.049	0.619	0.154	-0.186	1.183	11.381	141O-144N	1	1	1	1	1	7.427	11.565	8.428	-14.917	6.049	7.844
	3vb7				PRD_000913	M4Z	P	49	Mic is not modeled.	0.553	-0.032	-1.220	0.338	-1.550	141O-144N	1	1	1	1	1	7.624	11.529	6.997	0.769	0.387	0.249	0.899	11.965	141O-144N	1	1	1	1	1	7.653	11.385	8.329	-13.757	8.092	8.244
	4mds				23H	7		6.2*	V303A. C-terminal 3 residues do not exist.	0.508	-0.435	0.952	1.937	-1.091	141O-144N	1	1	1	1	1	7.594	11.103	6.585															0	-1.317	6.313
	4tww	R188I			3A7	41		63*	Non-covalent (distance between 3A7 and C145 is 2.3Å in chain A and 2.4Å in chain B). R188I prevents from proteolysis and increases the activity.	0.199	-0.368	0.096	-2.507	-9.745	141O-144N	1	1	1	1	1	7.535	11.050	6.746	0.401	0.021	0.303	-0.061	2.633	141O-144N	0	1	1	1	1	7.574	11.031	8.845	-8.363	-1.021	6.310
	4twy	R188I			3BL	40		108*	R188I prevents from proteolysis and increases the activity.	0.490	0.582	-0.566	0.598	7.188	141O-144N	1	1	1	1	1	7.664	11.165	7.704															-0.001	7.018	7.849
	4wy3	R188I			3X5	44		240*	Non-covalent (distance between 3X5 and C145 is 2.5Å). R188I prevents from proteolysis and increases the activity.	0.525	0.593	-0.832	1.118	7.545	141O-144N	1	1	1	1	1	7.829	11.423	7.62															0	7.262	8.092
	5b6o_A	C145A			C-term of another chain A		P		Chain A binds a symmetrically related chain A (301-310), while chain B is in free state. After C-term, GKFKKIVKGT are added. C145A makes the protein inactive.	0.587	0.835	-0.821	0.884	-23.013	141O-144N	1	1	1	1	1	7.385	11.113	7.364															-21.195	-3.44	6.189
	5c5n	R188I			SLH	phenyl-beta-alanyl (R,S)-N-decalin type inhibitor		275*	R188I prevents from proteolysis and increases the activity.	0.463	0.693	-0.672	1.817	7.759	141O-144N	1	1	1	1	1	7.773	11.261	7.674															0.002	7.618	7.851
	5c5o	R188I			SDJ	phenyl-beta-alanyl (S,R)-N-decalin type inhibitor		215*	R188I prevents from proteolysis and increases the activity.	0.299	-0.197	0.147	-2.599	-12.742	141O-144N	1	1	1	1	1	7.519	10.979	6.417	0.401	0.040	0.322	-0.367	4.554	141O-144N	1	1	1	1	1	7.467	10.937	8.909	-10.587	-3.132	6.253
	5n19				D03		P			0.522	0.939	-0.886	2.081	6.459	141O-144N	1	1	1	1	1	7.686	11.221	7.543															0	6.165	8.122
	5n5o				8O5		P			0.654	0.975	-0.262	-0.250	4.475	141O-144N	1	1	1	1	1	7.550	11.299	7.401															0	3.436	7.899
	6lnq				EJF	M7	P			0.850	1.020	-0.097	0.470	4.736	141O-144N	1	1	1	1	1	7.575	11.363	7.489															0.001	3.887	8.022
	6lny				EOC	8a (M15)	P	0.508*		0.787	0.731	-0.091	0.256	5.136	141O-144N	1	1	1	1	1	7.490	11.296	7.344															0.001	4.135	8.078
	6lo0				EOF	8b (M14)	P	0.830*		0.816	1.368	0.441	-2.230	4.580	141O-144N	1	1	1	1	1	7.471	11.247	7.488															0	3.031	8.035
	6w2a		MHHHHHH	MHHHHHH(-1) of A,B	VDJ/QYS	7j		1.1*	Sulfoxide of 7j is replaced by Sg of C145. The two ligands are stereoisomers, and cannnot be distinguished after binding. C-terminal 3 residues do not exist. Highly heterogeneous crystal environment of P 1 21 1.	0.485	1.004	-0.022	-3.233	-7.187	141O-144N	1	1	0	1	1	7.246	10.969	6.41	0.346	0.902	-0.302	-2.652	22.177	141O-144N	1	1	1	1	1	7.871	11.761	9.456	-20.855	9.505	6.884
	6w79				X77	X77				0.496	0.329	-1.274	1.296	6.618	141O-144N	1	1	1	1	1	7.801	11.379	7.671															0.001	6.13	8.256
	6wco				X47	X47				0.571	0.571	-1.437	1.448	6.294	141O-144N	1	1	1	1	1	7.836	11.534	7.736															-0.002	7.613	8.217
	6xhl		G	GS of A,B	V2M	4	P	0.004*, 5^{+}	Highly heterogeneous crystal environment of P 1 21 1.	0.333	1.432	0.860	-2.811	-10.014	141O-144N	1	1	0	1	1	7.560	11.421	6.348	0.351	1.139	0.467	-2.708	42.960	141O-144N	1	1	0	1	1	7.757	11.690	9.131	-38.32	20.824	9.541
	6xhn		G	GS of A, GSG of B	V3D	28	P	0.017*	Highly heterogeneous crystal environment of P 1 21 1.	0.384	1.627	0.376	-2.882	-4.269	141O-144N	1	1	0	1	1	7.505	11.329	6.444	0.304	1.636	0.099	-3.092	41.826	141O-144N	1	1	0	1	1	7.645	11.503		-34.819	23.401	10.082
	6xho		G	GS of A, GSG of B	V34	2	P		Highly heterogeneous crystal environment of P 1 21 1.	0.333	1.707	0.919	-3.474	-7.808	141O-144N	1	1	0	1	1	7.591	11.513	6.326	0.340	1.366	-0.032	-3.001	34.138	141O-144N	1	1	0	1	1	7.809	11.682		-31.549	15.747	7.795
	6y7m				OEW	13a	P			0.592	0.845	-0.904	1.219	1.878	141O-144N	1	1	1	1	1	7.575	11.323	7.25															0.001	1.258	7.271
SARS-CoV-2%	6lu7				PRD_002214	N3	P	16.77^{+}		0.810	0.732	-0.909	-1.766	-5.522	141O-144N	1	1	1	1	1	7.303	11.101	6.421															0	-11.704	5.314
	6lze				PRD_002347	11a	P	0.053*	C-terminal 3 reidues do not exist.	0.845	0.314	-0.773	1.870	-8.648	141O-144N	1	1	1	1	1	7.466	11.174	6.328															0.001	-12.306	5.355
	6m0k				PRD_002349	11b	P	0.040*	C-terminal 2 residues do not exist.	0.832	0.348	-0.023	1.907	-8.517	141O-144N	1	1	1	1	1	7.492	11.197	6.403															0	-11.853	5.366
	6m2n_AC				3WL	Baicalein		0.94*	Tetramer (two asymmetric dimers).	0.623	-0.172	-0.280	-0.496	0.217	141O-144N	1	1	1	1	1	7.471	11.322	7.116	0.764	-0.407	0.323	1.063	-4.649	141O-144N	1	1	1	1	1	7.642	11.302	6.911	-0.03	-1.811	5.429
	6m2n_BD				3WL	Baicalein				0.632	-0.152	-0.226	-0.650	1.125	141O-144N	1	1	1	1	1	7.454	11.198	7.257	0.755	-0.243	0.211	1.436	-4.548	141O-144N	1	1	1	1	1	7.682	11.431	7.004	1.358	-1.292	5.608
	6w63				X77	X77				0.576	-1.331	-0.820	0.274	-7.867	141O-144N	1	1	1	1	1	7.526	11.098	6.404															-0.001	-9.567	5.684
	6wnp				PRD_002382	Boceprevir	P			0.706	0.326	-0.471	-0.537	-2.562	141O-144N	1	1	1	1	1	7.716	11.332	6.799															0.001	-4.702	5.614
	6wtj				K36	GC376	P	0.19*	Sulfoxide is replaced by Sg of C145. Upon binding to C145, the prodrug, GC376, is converted to GC373.	0.997	-0.759	-0.548	-2.950	-8.744	141O-144N	1	1	1	1	1	7.409	11.218	6.283															0	-10.198	5.350
	6wtk				UED	GC373	P	0.40*, 1.5^{+}		0.936	-0.131	-0.554	-2.714	-8.547	141O-144N	1	1	1	1	1	7.340	11.261	6.35															0.001	-11.494	5.220
	6wtt_AA				K36	GC376	P	0.03* 3.37^{+}	Tetramer. Chain A is symmetric, while chain B&C are assymmetric. Sulfoxide in K36 is replaced by Sg of C145. Upon binding, GC376 becomes K36 in chain A&B and B1S (stereoisomer of K36) in chain C. After 304, 6 His are added.	1.270	0.919	-0.157	1.061	-4.006	141O-144N	1	1	1	1	1	7.364	10.897	6.17															-0.001	-8.032	5.262
	6wtt_BC				K36, B1S	GC376				1.444	-0.069	-0.329	1.382	-9.852	141O-144N	1	1	1	1	1	7.186	11.036	6.293	1.397	-0.673	-1.046	-0.744	-12.140	141O-144N	1	1	1	1	1	7.314	10.892	6.618	1.459	-11.265	5.024
	6xa4		HM	HMS	PRD_002391	calpain inhibitor II	P	0.97*		0.919	-0.870	0.378	-2.261	-12.065	141O-144N	1	1	0	1	1	7.785	11.646	6.734															-0.001	-9.569	5.410
	6xb1				NEN				C145 is di-oxydized, 2CO (SOO), and C156 is capped by NEN.	0.608	-1.803	-1.380	-2.465	-2.332	141O-144N	1	1	1	1	1	7.904	11.778	6.46															0	-4.951	5.556
	6xb2				NEN				C145 and C156 are capped by NEN.	0.639	-1.802	-1.042	-2.207	-1.586	141O-144N	1	1	1	1	1	7.644	11.596	6.487															0	-4.277	5.611
	6xbg		HM	HMS of A, HMSG of B	PRD_002392	UAW246	P	0.045* 15.13^{+}	Highly heterogeneous crystal environment of P 1 21 1.	0.604	0.913	0.382	-2.689	-10.519	141O-144N	1	1	0	1	1	7.614	11.309	6.113	0.293	1.053	-0.967	-0.113	33.895	141O-144N	1	1	0	1	1	7.696	11.431		-31.358	14.717	7.416
	6xbh		HM	HMS	PRD_002393	UAW247	P	0.045* 6.81^{+}		1.104	-1.412	-0.486	-2.591	-13.650	141O-144N	1	1	0	1	1	7.539	11.261	6.584															-0.001	-11.172	5.215
	6xbi		HM	H of A	PRD_002394	UAW248	P	20.49^{+}		0.644	0.874	-1.776	0.654	-11.376	141O-144N	1	1	0	1	1	7.434	11.366	6.312	1.030	1.224	-2.310	1.442	-9.291	141O-144N	1	1	0	1	1	7.531	11.248	7.375	-0.21	-7.152	5.476
	6xch				PRD_000216	Leupeptin	P	92*		0.664	-0.049	-0.661	-1.849	-9.910	141O-144N	1	1	1	1	1	7.882	11.630	6.5															0	-13.895	5.346
	6xfn		HM	HMS		calpain inhibitor XII	P	0.453*		0.137	-2.309	-0.315	-2.766	-3.527	141O-144N	1	1	0	1	1	7.887	11.413	7.384															0.001	-0.995	5.746
	6xhm				V2M	4	P	0.00027	Highly heterogeneous crystal environment of P 1 21 1.	0.563	1.214	1.455	-2.823	-15.900	141O-144N	1	1	1	1	1	7.557	11.418	6.387	0.423	1.510	0.709	-3.217	32.433	141O-144N	1	1	1	1	1	7.787	11.775	9.178	-34.993	9.904	6.982
	6xmk		SNIG	SNIGSGF of A, SNIG of B	QYS	7j	P	0.45*	Q306 do not exist. Highly heterogeneous crystal environment of P 1 21 1.	0.668	0.422	0.735	-2.507	-13.981	141O-144N	1	1	0	1	1	7.307	10.998		0.658	0.457	-0.168	-2.528	42.060	141O-144N	1	1	0	1	1	7.431	11.221	9.52	-38.069	19.635	8.892
	6xoa_AC	C145S			C-term of another protein		P		Tetramer (two asym dimers AB and CD). Chains A&C bind symmetrically related C-term of C&A, respectively. Dimer data are of AB. Chains B&D are free. C145S makes the protein inactive.	0.799	-0.531	1.075	1.935	-11.780	141O-144N	1	1	1	1	1	7.769	11.468	6.37	0.795	0.599	0.242	0.255	-2.678	141O-144N	1	1	1	1	1	7.478	11.202	6.46	-16.415	-2.912	5.273
	6xqs				SV6	Telaprevir	P	18*		0.586	0.343	-0.285	-1.472	0.222	141O-144N	1	1	1	1	1	7.785	11.312	6.593															0	-3.656	5.998
	6xqt				NNA	Narlaprevir	P	5.1*		1.014	-0.093	-0.104	-2.576	-10.810	141O-144N	1	1	1	1	1	7.733	11.354	6.472	0.833	1.074	-1.062	-2.523	-9.538	141O-144N	1	1	1	1	1	7.720	11.430	6.464	-1.011	-12.379	5.658
	6xqu				PRD_002382	Boceprevir	P	3.1*		0.772	1.803	-1.035	-1.535	-8.750	141O-144N	1	1	1	1	1	7.670	11.423	6.512															0.001	-13.286	5.313
	6xr3				V7G	GRL-024-20	P			0.504	0.764	-0.505	-2.556	-1.300	141O-144N	1	1	1	1	1	7.717	11.390	6.595															0	-4.239	5.540
	6y2f				O6K	13b	P	0.67* 4-5^{+}		0.991	0.791		1.606	-5.243	141O-144N	1	1	1	1	1	7.295	10.972	6.357															0.001	-8.942	5.209
	6y2g				O6K	13b	P	0.67* 4-5^{+}		0.954	1.489	-0.209	0.899	-0.775	141O-144N	1	1	1	1	1	7.399	11.270	7.158	1.199	2.009	0.557	1.410	-12.923	141O-144N	1	1	1	1	1	7.423	11.273	6.823	6.551	-3.949	5.227
	6ynq				P6N	2-Methyl-1-tetralone		24.05^{+}	HEAT is cleaved into 2-Methyl-1-tetralone and Tyramine. EC50 is for HEAT.	0.884	-1.053	-1.476	-0.541	-5.978	141O-144N	1	1	1	1	1	7.729	11.527	6															0.001	-9.846	5.183

	6yvf				A82	AZD6482			A82 is on the molecualr surface, which is not contained in the major binding sites.	0.880	-0.551	-1.436	0.332	-5.541	141O-144N	1	1	1	1	1	7.731	11.584	6.473															0.001	-8.7	5.308
	6z2e				Q5T	biotin-PEG(4)-Abu-Tle-Leu-Gln-vinylsulfone	P		Q5T contain a long polyether chain.	0.859	0.838	0.051	-1.018	-2.176	141O-144N	1	1	1	1	1	7.427	10.983	6.321															0.001	-4.654	5.671
	6zrt				PRD_002448	Telaprevir	P	55.76*		0.776	0.330	-0.340	-1.444	1.028	141O-144N	1	1	1	1	1	7.567	11.482	6.483															0	-2.954	5.783
	6zru				PRD_002382	Boceprevir	P	1.59*		0.852	1.447	-0.563	-1.332	-11.195	141O-144N	1	1	1	1	1	7.611	11.594	6.37															-0.001	-14.568	5.172
	7aku				RN2	Calpeptin		0.072[+]		0.643	-0.113	-1.265	-2.456	-9.968	141O-144N	1	1	1	1	1	7.552	11.144	6.165															-0.001	-10.285	5.499
	7b83				PK8	pyrithione zinc			PK8 covalently binds both C145 and H41 at Zn.	1.020	-0.909	-1.713	-0.256	-6.838	141O-144N	1	1	1	1	1	7.756	11.595	6.297															0	-10.158	5.175
	7bqy				PRD_002214	N3	P	16.77[+]	Ligand binding is improved over 6lu7.	0.798	1.130	-1.121	-0.430	-3.718	141O-144N	1	1	1	1	1	7.378	11.151	6.5															0	-8.561	5.435
	7brp		G	G of A,B	PRD_002382	Boceprevir	P	8.0*		1.102	3.712	-0.151	-1.539	-12.159	141O-144N	1	1	1	1	1	7.650	11.712	6.408	1.301	3.165	0.697	-0.988	-14.419	141O-144N	1	1	1	1	1	7.611	11.724	6.458	1.075	-14.237	5.518
	7buy				JRY	Carmofur		1.82* 24.30[+]	The fluorouracil moiety of carmofur is eliminated to make JRY upond binding.	0.441	0.202	0.481	1.601	-7.960	141O-144N	1	1	1	1	1	7.560	11.219	6.501															0.002	-11.529	5.270
	7c6s				PRD_002382	Boceprevir	P	8.0*		0.689	0.558	0.273	-1.000	-4.263	141O-144N	1	1	1	1	1	7.666	11.444	6.598															0.001	-6.71	5.476
	7c6u				K36	GC376		0.15*	Sulfoxide is replaced by Sg of C145.	1.050	0.649	-0.039	-1.400	-10.703	141O-144N	1	1	1	1	1	7.297	11.162	6.203															0	-13.249	5.552
	7c7p				PRD_002448	Telaprevir	P		Almost a half of PRD_002448 is missing in chain B, and named FK3, while it is fully modeled in chain A.	0.510	0.706	-0.844	-0.428	3.052	141O-144N	1	1	1	1	1	7.770	11.324	6.887	0.746	0.404		1.973	-3.453	141O-144N	1	1	1	1	1	7.646	11.384	6.51	-0.455	-2.592	5.356
	7c8b				PRD_002352	Z-VAD (OMe)-FMK	P			0.524	0.064	-0.754	2.114	-5.474	141O-144N	1	1	1	1	1	7.850	11.617	6.745															-0.001	-8.732	5.313
	7c8r				TG3	TG-0203770	P			0.587	2.254	0.015	0.779	0.790	141O-144N	1	1	1	1	1	7.410	11.093	6.349															-0.001	-5.224	5.752
	7c8t				NOL	TG-0205221	P			0.895	1.518	-1.047	1.433	-1.767	141O-144N	1	1	1	1	1	7.556	11.113	6.295															0	-5.886	5.530
	7c8u			SG	K36	GC376	P		Sulfoxide is replaced by Sg of C145.	0.811	-0.524	-0.553	-2.401	-5.604	141O-144N	1	1	0	1	1	7.323	11.298																0	-6.932	5.607
	7cbt		27 res	27 res+ SGF of A,B	K36	GC376	P	0.643[+] 0.881[+]	Sulfoxide is replaced by Sg of C145.	0.896	0.602	0.816	-2.104	-4.228	141O-144N	1	1	0	1	1	7.460	10.963		0.774	0.615	0.606	-1.354	2.620		1	1	0	1	1	7.542	11.217		-3.417	0.837	5.545
	7com				PRD_002382	Boceprevir	P			0.674	0.488	-0.462	1.660	2.253	141O-144N	1	1	1	1	1	7.854	11.507	6.907	0.819	0.191		1.942	-3.242	141O-144N	1	1	1	1	1	7.797	11.516	6.851	-0.504	-2.223	5.446
	7cx9				GKF	INZ-1				0.214	1.000		1.389	-4.238	141O-144N	1	1	1	1	1	8.053	11.962	6.732															-0.001	-8.227	5.137
	7d1m		G	GS of A, GSG of B	K36	GC376	P	0.15*	Sulfoxide is replaced by Sg of C145. Highly heterogeneous crystal environment of P 1 21 1.	0.833	0.791	0.592	-2.880	-12.259	141O-144N	1	1	0	1	1	7.362	11.082	8.549	0.349	0.554	0.029	-2.161	31.074	141O-144N	1	1	0	1	1	7.454	11.396		-31.017	13.809	6.972
	7d1o				NNA	Narlaprevir	P	16.11*		1.196	0.667	0.236	-1.369	-16.306	141O-144N	1	1	1	1	1	7.506	11.658	6.491															-0.002	-13.997	5.564
	7d3i				GQU	MI-23	P	0.0076*	GQU is hydrogen bonded with S1 of chain B.	1.280	2.294	-1.533	0.015	-8.860	141O-144N	1	1	1	1	1	7.479	11.172	6.335															-0.001	-9.409	5.493
	7jkv		G	G of A	V7G	5h	P	0.0176 4.2[+]	Highly heterogeneous crystal environment of P 1 21 1.	0.248	1.751	0.531	-3.052	-10.714	141O-144N	1	1	0	1	1	7.506	11.311	6.666	-0.012	1.283	0.479	-3.065	38.703	141O-144N	1	1	1	1	1	7.729	11.566	9.737	-33.707	18.045	7.974
	7joy_B	C145A			C-term of another chain B		P		Chain B binds a symmetrically related C-term, while chain A are in free state. C145A makes the protein inactive.															0.844	0.369	-0.369	0.808	8.088	141O-144N	1	1	1	1	1	7.298	10.675	7.975	-1.691	5.914	5.965
	7ju7				G65	Masitinib		2.6,2.5* 2.1[+],3.2[+]		0.455	0.378	-0.314	1.819	-7.308	141O-144N	1	1	1	1	1	7.784	11.370	6.596															0	-11.037	5.484
	7jyc				NNA	Narlaprevir	P			1.214	0.992	-1.365	-2.237	-13.017	141O-144N	1	1	1	1	1	7.528	11.504	6.252															0	-15.669	5.428
	7k40				PRD_002382	Boceprevir	P			0.872	2.636	-0.879	-1.686	-12.475	141O-144N	1	1	1	1	1	7.539	11.449	6.151															0	-17.424	5.113
	7k6d				PRD_002448	Telaprevir	P		Acoustic droplet ejection. Cryo-protected.	0.713	0.494	-0.368	-1.482	0.183	141O-144N	1	1	1	1	1	7.673	11.389	6.485															0	-4.091	6.131
	7k6e				PRD_002448	Telaprevir	P		Acoustic droplet ejection. Direct vitrification.	0.599	0.531	-0.223	-1.323	1.348	141O-144N	1	1	1	1	1	7.618	11.448	6.517															0	-3.897	6.040
	7khp_B				C-term of another chain B		P		Chain B binds a symmetrically related C-term, while chain A are in free state. Q306 forms a covalent bond with C145 to form the acyl-enzyme intermediate.															0.836	0.939	-0.173	1.437	9.127	141O-144N	1	1	1	1	1	7.579	11.183	7.356	-3.358	5.057	5.710
	7lfp		GAM	GAM of B	XY4	F2X Entry Library G05 fragment			A single XY4 is at the protomer interface between the two N-fingers, and located out side the major binding sites.	-1.680	-0.364	0.029	1.703	8.856		1	0	0	1	0	13.658	8.634	10.043	-10.861	1.054	2.326	2.327	10.531	139O-142N	0	0	0	0	0	9.802	13.847	7.971	-3.084	17.418	9.847
	7nev				PRD_000216	Leupeptin	P			1.119	0.767	-0.509	0.180	-14.576	141O-144N	1	1	1	1	1	7.569	11.364	6.375															0	-15.051	5.156

PDB data are of the version of 10/25/2020. Lightgray colored cells indicate either chain B of symmetric dimer or ligand-unbound chain. Distances are in Å.

[$]Peptide or peptide-mimic ligand is defined when a ligand contains more than or equal to two peptide moieties. However, it is admitted that a carbonyl group is replaced by alcohol, and that Cα is in a part of an aromatic group.

[#]The residues with underline indicate that they are of the native sequence.

[%]Data from the PanDDA analysis (115entries) and the entry having swapping, 3iwm, were not used in this study.

[&]HBs: 1 for formed and 0 for not formed. HBs are intra-protomer hydrogen bonds except HB 140-1.

Dataset S2. Summary of the ligand-free entries.

specirs	protein				comments	chain A													chain B												dimer		
						PC1					C-loop conformation									PC1					C-loop conformation										
	PDB ID	mutation	residues added to N-term	missing N-term residues		C-loop	E-loop	helical loop	linker	Domain III	main-chain HB within 138-144	HB 138-172[&]	HB 139-126[&]	HB 140-1[&]	HB 141-118[&]	HB 143-28[&]	distance 165Cα-140Cβ	distance 165Cα-141Cβ	distance 2-214	C-loop	E-loop	H-loop	Linker	Domain III	main-chain HB within 138-144	HB 138-172[&]	HB 139-126[&]	HB 140-1[&]	HB 141-118[&]	HB 143-28[&]	distance 165Cα-140Cβ	distance 165Cα-141Cβ	distance 2-214	PC1 Domain III	PC2 Domain III	distance between two 285 Cα's
SARS-CoV[%]	1q2w	F305E, Q306G	SL	SLSG of A		0.278	0.087		1.137	5.219	141O-144N	1	1	0	1	1	7.650	11.874		0.463	0.272		1.729	15.065	141O-144N	1	1	0	0	1	7.408	11.805	8.684	-10.325	12.841	8.717
	1uj1			SG of A		0.347	-0.304	0.121	2.396	15.308		1	1	1	1	1	8.024	12.716		-7.437	-2.501	-0.408	-1.858	1.369	138O-141N 139O-142N	0	0	0	0	0	13.326	7.826	7.495	12.888	14.396	8.446
	1uk2					-0.739	-1.139	-0.188	0.027	6.582		0	0	1	0	1	9.119	13.142	8.081	-4.879	-2.099	-0.724	0.412	1.699	138O-140N	0	0	0	0	0	9.335	14.134	6.703	6.776	11.641	10.291
	1uk3			SG of A		-0.456	-1.656	1.736	0.147	10.022		1	0	0	0	1	8.949	13.583		-3.759	-1.666	0.009	1.131	1.041	138O-140N 139O-141N	0	0	0	0	0	11.552	11.767	7.765	9.945	12.545	10.300
	1z1i					1.164	-3.305	-0.087	0.735	-12.480	141O-143N 141O-144N	1	1	1	1	1	7.888	11.419	7.047														0	-8.503	6.615
	1z1j_B	C145A			Chain A binds a symmetrically related chain A (301-306) while chain B is in free state. C145A makes the protein inactive.															0.260	-0.254	-0.343	1.299	-7.947		0	1	0	1	1	8.076	12.230	6.572	8.53	1.861	5.767
	2a5a					0.557	0.173	-0.104	1.668	4.216	141O-144N	1	1	1	1	1	8.060	11.824	7.389														0.001	4.883	7.323
	2bx3			S		-6.466	-1.075	1.136	1.481	6.677	138O-140N 141O-144N	0	0	0	0	0	12.959	7.929	8.47														-0.001	10.701	8.055
	2bx4			SG		-5.559	-2.370	-0.629	-0.376	-1.983	138O-140N 141O-144N	1	0	0	0	0	12.447	7.681															0	0.356	6.472
	2c3s					0.556	-3.945	-0.031	-0.420	-3.520	141O-144N	0	0	0	0	1	7.637	11.672	8.194														-0.001	0.362	6.628
	2duc					0.530	0.545	0.847	2.152	12.658	141O-144N	1	1	1	1	1	7.956	11.716	7.065	-4.531	-0.173	-0.302	-1.623	2.899	141O-144N	1	0	0	0	0	8.448	12.633	7.338	11.684	10.101	8.463
	2gt7					0.718	0.147		2.076	10.744	141O-144N	1	1	1	1	1	7.929	11.755	8.381	0.443	0.136	-0.016	1.249	2.885	141O-144N	1	1	1	1	1	8.079	11.894	7.314	10.657	9.188	8.313
	2gt8		A	ASG		-7.697	-1.377	1.613	1.098	7.986	138O-140N 141O-144N	0	0	0	0	0	12.958	7.926															-0.001	11.365	9.131
	2gz9					0.480	0.486	-0.499	1.540	4.689	141O-144N	1	1	1	1	1	7.810	11.646	7.581														0.001	6.026	7.767
	2h2z					0.609	0.576	-0.399	1.206	6.193	141O-144N	1	1	1	1	1	8.137	11.908	7.749														0.001	6.409	7.968
	2qc2	N214A	GS	G of A,GS of B	N214A breaks HB 214-2 to destabilizes the active state.	-0.259	-0.581	-0.306	2.760	12.571		1	0	0	0	0	7.604	11.472	8.266	-1.561	-2.854	0.317	0.526	0.061		0	0	0	1	1	7.848	12.251	7.151	10.82	9.722	8.557
	3aw1	R188I			R188I prevents from proteolysis and increases the activity.	0.684	-1.739	-0.546	-1.844	-2.379	141O-144N	1	1	1	1	1	7.808	11.947	6.922	0.529	0.038	-0.815	1.092	12.289	141O-144N	1	1	1	1	1	8.094	11.934	7.807	-9.809	4.175	7.926
	3e91	S284A,T285A,I286A			T285A is the same mutation as SARS-CoV-2 3CLpro.	0.382	-0.287	0.326	1.146	8.903	141O-144N	1	1	1	1	1	7.372	11.395	8.14	0.190	-1.063	0.426	0.629	-9.126	141O-144N	1	1	0	1	1	7.458	11.224	6.973	14.701	0.145	6.367
	3ea7	S284A,T285A,I286A			T285A is the same mutation as SARS-CoV-2 3CLpro.	0.694	-0.058	-1.132	2.346	3.286	141O-144N	1	1	1	1	1	7.669	11.758	7.767	0.404	-0.861	-0.985	0.975	-10.042	141O-144N	1	1	1	1	1	7.502	11.572	6.493	14.459	-0.552	6.180
	3ea8	S284A,T285A,I286A			T285A is the same mutation as SARS-CoV-2 3CLpro.	0.345	0.241	-0.507	1.547	0.616	141O-144N	1	1	1	1	1	7.632	11.385	7.216															-0.001	-0.411	5.375
	3ea9	S284A,T285A,I286A,F291A			T285A is the same mutation as SARS-CoV-2 3CLpro.	0.566	-0.225	-1.043	1.166	-6.287	141O-144N	1	1	1	1	1	7.326	11.163	7.239															-0.001	-9.603	5.356
	3eaj_AC	S284A,T285A,I286A,F291A			Chains A&C and B&D are two symmetric dimers. T285A is the same mutation as SARS-CoV-2 3CLpro.	0.537	-0.596	-1.486	0.314	-6.363	141O-144N	1	1	1	1	1	7.113	11.011	6.576															0.001	-10.259	8.074
	3eaj_BD	S284A,T285A,I286A,F291A			T285A is the same mutation as SARS-CoV-2 3CLpro.	0.723	-0.272	-1.28	0.93	-2.966	141O-144N	1	1	1	1	1	7.822	11.887	6.366															0	-8.14	5.234
	3f9f	F140A	GS	GSS of A,B	F140A breaks the hydrophobic interactions with H163 and H172 to destabilize the active state.	-10.938	-2.379	-0.315	-1.933	-2.022	139O-143N 141O-144N	0	0	0	0	0	10.416	13.537	7.482	-11.237	0.089	-0.386	0.196	-1.197	139O-143N 141O-144N	0	0	0	0	0	10.181	13.384	8.51	-0.483	-0.429	9.456
	3f9g	F140A	GS	GSS of A,GSSG of B	C-terminal 5 residues do not exist. F140A breaks the hydrophobic interactions with H163 and H172 to destabilize the active state.	-8.002	-1.266	-0.389	-0.222	-0.990		0	0	0	0	0	12.698		9.47	-8.184	-3.168	-0.224	-1.945	-1.179		1	0	0	0	0	9.547			-0.187	0.609	9.756
	3f9h	F140A	GS	GSS of A, GS of B	F140A breaks the hydrophobic interactions with H163 and H172 to destabilize the active state.	-11.189	-1.867	-0.628	-2.651	-1.228		0	0	0	0	0	11.559	14.061	7.399	-11.715	-0.211	-0.154	-0.117	-1.160		0	0	0	0	0	13.090	13.823	8.472	0.339	-0.118	9.720
	3fzd	N28A		SG	N28A breaks both HB 145-28 and HB 143-28 to destabilize the active state. Residues 139-141 in C-loop are missing. C145 and C117 has S-S bond. C-terminal 5 residues do not exist.		-3.991	0.485	-0.570	-18.669		0	0	0	0	0																	-0.001	-12.071	6.906
	3m3s	N214A			N214A breaks HB 214-2.	0.785	-0.214	-1.060	2.191	9.714	141O-144N	1	1	1	1	1	7.802	11.773	8.58	-0.011	0.197	-0.513	1.231	4.544	141O-144N	1	1	1	1	1	8.016	11.816	7.871	8.248	10.49	8.370
	3m3v	S284A,T285A,I286A	GS	GS of A, G of B	T285A is the same mutation as SARS-CoV-2 3CLpro.	-0.041	-0.655	-0.438	1.384	6.051		1	1	0	1	0	7.790	11.864	8.546	-0.281	-1.883	0.028	1.992	-8.071		0	0	0	1	1	7.841	11.445	6.991	11.989	1.341	6.898
	3vb3					0.425	-1.155	-1.111	0.253	-10.374	141O-144N	1	1	1	1	1	7.958	12.034	6.587	0.454	0.117	2.655	2.291	6.127	141O-144N	1	1	1	1	1	7.761	11.672	8.143	-13.491	1.334	6.698
	4hi3	R298A	M	M of A, B	R298A impairs dimerization. Crystalized with 1mM substrate (ligand induced dimerization), but still density was not observed. After C-term, LE+6His are added.	0.477	-0.544	0.333	1.012	2.519	141O-144N	1	1	1	1	1	7.456	11.379	10.639	0.205	-0.557	0.937	-1.804	-9.058	141O-144N	1	1	1	1	1	7.484	11.111	6.61	7.898	2.832	6.455
	5b6o_B	C145A			Chain A binds a symmetrically related chain A (301-310), while chain B is in free state. C145A makes the protein inactive.															0.410	0.098	0.735	0.995	6.439	141O-144N	1	1	1	1	1	8.158	11.982	7.478	-21.195	-3.44	6.189
mono	2pwx	G11A	GS	GSGSF	Monomeric in crystal. G11A destroys the tight binding in the dimerization interface.	-7.626	-2.426	1.488	4.155		138O-141N 139O-142N	0	0		0	0	14.180	8.704																		
	2qcy	R298A			Monomeric in crystal. R298A impairs dimerization.	-7.877	-1.606	0.993	3.573	-154.30	138O-141N 139O-142N 141O-144N	0	0		0	0	13.672	8.315	9.831																	
	3f9e	S139A	GS	GSSG	Monomeric in crystal. S139A impairs dimerization.	-7.866	-2.720	1.536	3.898	-156.16	138O-141N 139O-142N 141O-144N	0	0		0	0	14.541	9.141																		
	3m3t	R298A	GS		Monomeric in crystal.R298A impairs dimerization.	-7.400	-2.202	0.048	3.211	-153.83	138O-141N 139O-142N 141O-144N	0	0		0	0	14.174	8.847	10.111																	
SARS-CoV-2	6m03					0.611	-1.789	-0.808	-1.452	-6.662	141O-144N	1	1	1	1	1	7.614	11.577	6.314														-0.001	-8.573	5.227
	6m2q					0.798	-2.391	-1.098	-2.643	-4.920	141O-144N	1	1	1	1	1	7.689	11.762	6.422														0	-7.188	5.231
	6wqf					0.633	-1.865	-1.559	-2.187	-2.464	141O-144N	1	1	1	1	1	7.845	11.555	6.431														0.001	-5.765	5.684
	6wtm					0.978	-2.470	-1.268	-2.894	-5.314	141O-144N	1	1	1	1	1	7.297	11.335	6.481	0.928	-2.561	-1.036	-2.518	-6.130	141O-144N	1	1	1	1	1	7.380	11.334	6.161	1.098	-7.571	5.418
	6xb0				C145 is di-oxydized, 2CO (SOO).	0.672	-1.936	-1.468	-2.108	-2.746	141O-144N	1	1	1	1	1	7.723	11.519	6.387															0	-6.211	5.470
	6xhu					1.011	-2.824	-0.483	-2.575	-7.561	141O-144N 142O-144N	1	1	1	1	1	7.655	11.429	6.473	0.688	-2.151	-1.329	-3.017	-2.107	141O-144N	1	1	1	1	1	7.643	11.412	6.527	-2.874	-6.344	5.706
	6xkf				C145 is mono-oxydized, CSX.	0.616	-2.060	-1.318	-3.305	-3.840	141O-144N	1	1	1	1	1	7.333	11.385	6.658	0.557	-2.220	-1.292	-2.859	-5.935	141O-144N	1	1	1	1	1	7.537	11.452	6.252	1.856	-8.154	5.499
	6xkh				C145 is di-oxydized, CSD (OSO).	0.519	-0.321	0.488	2.373	-1.963	141O-144N	1	1	1	1	1	7.674	11.323	6.736															0	-1.966	5.265
	6xoa_BD	C145S			Tetramer (two asym dimers, AB&CD). Chains A&C bind symmetrically related C-term of C&A, respectively. Chains BD are free. Dimer data are of CD. C145S makes the protein inactive.	0.266	0.167	-1.656	0.317	3.339	141O-144N	1	1	1	1	1	8.027	11.767	7.227	0.860	0.160	-0.524	-0.133	1.765	141O-144N	0	1	1	1	1	7.510	11.278	6.245	-5.535	-3.383	5.805
	6y2e					0.765	-2.218	-1.382	-2.748	-5.350	141O-144N	1	1	1	1	1	7.745	11.778	6.350														-0.001	-8.21	5.216
	6y84					1.040	-1.365	-1.495	-0.534	-6.701	141O-144N	1	1	1	1	1	7.412	11.240	5.959														0	-11.786	5.077
	6yb7					1.077	-1.514	-1.486	-0.499	-6.374	141O-144N	1	1	1	1	1	7.447	11.361	5.947														0	-12.153	5.085
	7bro		G	GS		1.286	-4.201	0.826	-1.805	-13.749	141O-144N	0	0	0	0	1	7.656	11.822	8.738														0.001	-9.963	5.796
	7c2q	S1,G2 del	S1,G2 del	S1,G2 del	C-terminal 8 residues do not exist. Deletion of S1 and G2 imapirs dimerization.		-0.571	-0.118	2.372			1	1	0	0	1					-0.256		1.908			0	0	0	0	1				0.559	11.858	7.284
	7c2y			SGF of A, SG of B	C-terminal 8 residues do not exist.		-0.571	-0.128	2.240			1	1	0	0	0	7.824				-0.211		1.967			0	0	0	0	0				0.235	12.501	7.812
	7cwb				XFEL.	1.169	-3.185	-0.480	-2.704	-4.164	141O-144N	1	1	1	1	1	7.615	11.716	6.276														0	-7.107	5.623
	7cwc		GSHM	GSHM of A,GSHMSG of B	XFEL.	0.138	-1.094	-0.860	-0.261	9.187	141O-144N	0	0	0	1	1	8.272	12.225	9.149	0.706	-0.126	0.253	-0.267	1.260	141O-144N	0	1	0	1	1	7.911	11.829		3.31	14.361	8.884
	7jfq					0.617	-0.875	-1.219	0.549	-8.191	141O-144N	1	1	1	1	1	7.971	11.825	6.581														-0.002	-8.645	5.296
	7joy_A	C145A			Chain B binds a symmetrically related C-term of chain B, while chain A are in free state. C145A makes the protein inactive.	0.528	0.078	-0.005	0.484	5.424	141O-144N	1	1	1	1	1	7.365	10.859	6.533															-1.691	5.914	5.965
	7jp1					0.874	-1.179	-1.955	-0.886	-3.401	141O-144N	1	1	1	1	1	7.860	11.797	6.437														-0.002	-7.179	5.272
	7jr3					0.512	0.199	0.205	1.933	-7.733	141O-144N	1	1	1	1	1	7.681	11.348	6.555														-0.001	-10.682	5.579
	7jr4				K61 is methylated, MLZ.	0.427	0.249		1.728	-7.280	141O-144N	1	1	1	1	1	7.587	11.343	6.525														0	-11.003	5.294
	7jun				Neutron diffraction determining the H positions.	0.816	-2.226	-1.164	-2.774	-3.892	141O-144N	1	1	1	1	1	7.595	11.466	6.499															-0.001	-5.745	5.586
	7jvz				XFEL.	0.542	-1.830	-1.301	-2.281	-3.543	141O-144N	1	1	1	1	1	7.700	11.720	6.652															-0.001	-3.708	5.849
	7k3t					1.200	-1.820	-1.498	-0.537	-6.848	141O-144N	1	1	1	1	1	7.277	11.381	5.717														0	-12.684	5.105
	7kfi		GAM	GAM of B		-1.587	-0.209	-0.341	1.858	11.263		0	0	0	1	0	14.216	9.164	10.172	-10.762	1.168	2.003	2.270	12.321	139O-142N	0	0	0	0	0	9.731	13.923	7.78	-3.175	19.214	9.858
	7khp_A				Chain B binds a symmetrically related C-term of chain B, while chain A are in free state.	0.498	0.364	0.231	0.525	3.636	141O-144N	1	1	1	1	1	7.583	11.273	6.507															-3.358	5.057	5.710

PDB data are of the version of 10/25/2020. Lightgray colored cells indicate either non-exsisting chain B of symmetric dimer or ligand-bound chains. Cells colored in darkgray are those with undetermined data due to missing residues. Distances are in Å.

[%]The entries containing only domain III, 2k7x, 2liz, and 3ebn, were not used in this study.

[&]HBs: 1 for formed and 0 for not formed. HBs are intra-protomer hydrogen bonds except HB 140-1.

Dataset S3. Ligand binding.

species	PDBid	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker						Ligand interactions	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker						Ligand interactions
		BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192		BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	
SARS-CoV	1uk4	A	1	0	0	1	1	0	11	1	1	1	11	21	11	0	1	11	0	0	1	0	0	11	0	0	1	CE	B	1	0	0	11	1	0	0	0	0	1	1	21	0	1	1	11	0	1	0	0	11	1	11	0	11	HL
	1wof	A	1	1	0	1	1	0	1	1	1	1	0	21	11	11	1	11	0	1	1	1	1	11	11	1	1	CEL	B	0	1	0	1	1	0	1	0	1	11	0	21	11	11	1	11	0	1	1	1	1	11	11	1	1	CEL
	1z1j	A	0	0	0	11	1	0	11	1	0	11	1	11	11	11	1	11	0	1	1	1	1	11	0	1	11	CEHL																											
	2a5i	AB	1	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	0	1	1	1	1	11	1	1	1	CEHL																											
	2a5k	A	1	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	1	0	1	1	1	11	1	0	1	CEHL	B	1	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	0	1	1	1	1	11	1	1	1	CEHL
	2alv	AB	0	1	1	1	0	1	11	1	1	1	0	21	11	11	1	11	0	1	1	1	1	1	1	1	1	CEL																											
	2amd	A	1	1	0	1	1	0	1	0	1	1	0	21	11	11	1	11	0	1	1	1	1	11	1	1	1	EL	B	1	1	1	1	1	0	1	0	1	1	0	21	11	11	1	11	0	1	1	1	1	11	1	1	1	REL
	2amq	A	1	1	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	1	11	11	1	1	CEL	B	1	1	1	1	0	0	1	0	0	1	1	21	11	11	1	11	0	1	1	1	1	11	11	0	1	REL
	2d2d	A	0	1	1	1	1	0	11	1	1	1	1	21	11	11	1	11	0	1	1	0	0	1	1	1	1	CEL	B	0	1	1	1	1	0	11	1	1	1	1	21	11	11	1	11	0	1	1	0	0	11	1	1	1	CEL
	2gtb	AB	1	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	1	1	1	1	1	11	1	0	1	CEHL																											
	2gx4	AB	0	0	0	1	1	1	11	0	0	11	0	21	11	11	1	11	1	1	1	1	1	11	1	1	1	CEHL																											
	2gz7	AB	0	0	0	1	0	0	0	0	0	0	0	1	0	1	1	1	0	0	0	1	1	0	0	0	1																											
	2gz8	AB	0	0	0	1	0	0	0	1	11	1	1	11	0	0	1	1	0	1	0	0	0	1	1	0	1	C																											
	2hob	AB	1	1	1	1	1	0	11	1	1	1	1	21	11	11	1	11	0	1	1	1	1	11	11	1	1	RCEL																											
	2op9	A	0	0	0	11	1	0	0	1	1	11	1	11	0	0	1	11	0	0	0	1	1	1	0	0	0	CH	B	0	0	0	11	1	0	0	1	0	11	1	21	0	1	1	11	0	0	0	1	1	0	0	0	0	CH
	2q6g	A	1	11	0	0	1	1	11	1	1	11	0	11	11	11	1	11	0	1	1	1	0	11	11	1	0	RCEL	B	1	11	1	1	1	1	11	1	1	11	0	11	11	1	1	11	0	1	1	1	1	11	11	0	1	RCEHL
	2qiq	AB	0	1	1	1	1	1	11	1	1	1	0	11	11	11	1	11	0	1	1	1	1	1	11	0	1	CEHL																											
	2v6n	AB	0	0	0	1	1	0	0	0	0	0	0	21	0	1	1	0	0	0	0	1	1	1	0	0	0																											
	2vj1	A	0	0	0	1	21	0	0	0	0	0	0	0	0	0	21	0	0	0	0	1	1	1	0	0	0	H	B	0	0	0	0	0	0	0	1	1	1	0	21	1	0	0	21	0	0	0	0	0	0	0	0	0	
	2z3c	AB	0	0	0	1	0	0	11	1	1	11	1	21	11	11	1	11	0	0	1	0	0	0	0	0	0	CE																											
	2z3d	AB	0	0	0	11	1	0	11	1	1	11	1	21	11	11	1	11	1	1	1	0	0	0	1	0	1	CEH																											
	2z3e	AB	0	0	0	1	1	0	11	1	1	11	1	21	11	11	1	11	1	1	1	0	0	11	1	0	1	CEL																											
	2z94	AB	0	0	0	1	0	0	0	0	1	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0																											
	2z9g	AB	0	0	0	1	1	20	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	1	0	0	0	H																											
	2z9j	A	0	0	1	1	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0		B	0	0	0	1	0	0	0	0	0	0	0	20	0	1	0	0	0	0	0	0	0	0	0	0	0	
	2z9k	A	1	0	1	1	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0		B	0	0	1	1	0	0	0	0	0	0	0	21	0	1	0	0	0	0	0	0	0	0	0	0	0	
	2z9l	A	0	0	0	1	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0		B	0	0	1	1	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2zu4	AB	1	1	1	1	1	0	11	1	1	11	0	21	11	11	1	11	0	1	1	1	0	11	1	1	1	RCEL																											
	2zu5	AB	1	1	1	1	1	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	0	11	1	1	1	RCEL																											
	3atw	A	0	0	0	1	1	1	1	1	1	11	1	11	11	11	1	11	1	1	0	1	1	1	11	1	0	CEHL	B	0	0	0	1	1	0	1	1	1	11	1	11	11	11	1	11	1	1	0	1	1	1	11	0	0	CEL
	3avz	AB	0	0	0	1	1	0	1	0	1	11	1	21	11	11	1	11	0	1	0	1	1	1	11	1	0	CEL																											
	3aw0	AB	0	0	0	1	1	0	1	1	1	1	1	11	11	1	1	11	0	1	0	1	0	0	0	1	1	CE																											
	3d62	AB	0	0	0	11	1	0	0	0	1	11	1	21	0	1	1	0	0	0	0	0	1	1	0	0	0	CH																											
	3sn8	AB	0	0	0	0	1	0	1	1	1	11	1	21	0	1	1	11	0	0	0	1	1	1	0	0	0	C																											
	3sna	AB	0	0	0	11	1	0	11	1	1	11	11	21	11	0	1	11	0	1	0	0	0	0	11	1	0	CEH																											
	3snb	AB	0	0	0	1	1	0	11	1	0	1	0	21	11	1	1	11	0	1	0	0	1	1	11	0	0	CEL																											
	3snc	AB	0	0	0	1	1	0	11	1	1	0	0	21	11	11	1	11	0	1	0	0	0	1	1	1	0	CE																											
	3snd	A	0	0	0	0	0	0	11	1	0	1	1	21	11	11	1	11	0	0	1	0	0	0	0	0	0	CE	B	0	0	0	0	1	0	11	1	1	11	0	21	11	11	1	11	0	0	0	1	0	0	0	0	0	CE
	3sne	AB	0	0	0	1	1	0	11	1	1	11	0	21	11	1	1	11	1	1	0	1	0	1	1	0	0	CE																											
	3szn	AB	0	1	1	1	1	0	11	1	1	11	1	21	11	11	1	11	0	0	1	1	1	1	0	0	0	CE																											
	3tit	AB	0	0	0	0	1	0	11	1	1	11	1	21	11	11	1	11	0	0	1	1	1	1	0	0	0	CE																											
	3tiu	AB	1	0	0	1	0	1	11	1	1	11	1	21	11	11	1	11	0	1	1	1	1	11	1	0	1	CEL																											
	3tns	AB	0	0	0	1	1	1	11	0	1	1	1	21	11	11	1	11	0	1	1	1	1	11	1	1	1	CEHL																											
	3tnt	AB	0	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	0	1	1	1	1	11	1	1	1	CEHL																											
	3v3m	AB	1	1	0	1	1	0	1	1	1	11	11	1	11	1	1	11	0	0	0	1	0	0	0	0	0	CE																											
	3vb4	A	0	0	1	1	1	0	11	1	0	0	0	21	11	11	1	11	1	1	1	1	1	11	11	1	1	CEL	B	0	0	0	1	1	1	11	11	0	0	1	21	11	11	1	11	1	0	1	0	0	11	11	1	0	CEHL
	3vb5	A	0	0	0	0	0	0	1	1	0	1	1	21	11	11	1	11	1	1	1	0	0	11	11	1	1	CEL	B	0	0	0	1	1	0	11	1	0	1	0	21	11	11	1	11	1	1	1	0	0	11	11	1	1	CEL
	3vb6	A	0	0	0	1	1	0	11	1	11	1	1	21	11	11	1	11	0	0	1	1	1	1	1	0	1	CEL	B	0	0	0	1	1	0	11	11	0	0	1	21	11	11	1	11	0	0	1	0	1	1	11	0	1	CEL
	3vb7	A	0	0	0	1	1	0	11	1	0	1	1	21	11	11	1	11	0	1	1	1	0	11	1	0	1	CEL	B	0	0	0	1	1	0	11	1	0	0	1	21	11	11	1	11	0	0	1	1	1	11	1	0	1	CEL
	4mds	AB	0	0	0	1	1	0	1	1	1	0	0	11	11	0	1	11	1	1	0	0	1	1	0	0	0	E																											
	4tww	A	0	0	0	1	1	0	1	1	1	11	1	11	11	11	0	1	0	0	0	1	1	1	0	0	0	CE	B	0	0	0	0	1	0	1	1	1	1	11	11	11	10	0	1	0	0	1	1	1	1	0	0	0	CE
	4twy	AB	1	0	0	1	1	0	1	1	1	11	1	21	11	10	0	1	0	0	0	1	0	0	0	0	0	CE																											
	4wy3	AB	0	0	0	1	1	0	1	1	1	1	1	11	11	1	1	1	0	0	1	1	1	1	0	0	0	CE																											
	5b6o	A	1	11	0	11	1	0	1	1	1	11	10	11	11	10	1	11	1	1	1	1	1	11	1	1	1	RCEHL																											

	5c5n	AB	0	0	0	1	1	0	1	1	1	11	0	21	11	1	1	1	0	0	0	1	1	1	0	0	0	C
	5c5o	A	1	0	0	1	1	0	1	1	1	11	11	21	11	10	0	1	0	0	0	1	1	1	0	0	0	CE
	5n19	AB	1	0	0	11	1	0	11	0	1	11	1	21	11	11	1	11	0	0	1	1	1	1	0	0	0	CEH
	5n5o	AB	0	1	0	11	0	0	11	1	1	11	0	21	11	11	1	11	0	0	1	1	0	11	1	0	0	CEL
	6lnq	AB	0	0	0	1	0	0	11	1	1	0	1	21	11	11	1	11	0	1	1	0	0	0	11	1	1	CEL
	6lny	AB	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	0	0	11	0	0	0	CE
	6lo0	AB	0	0	0	1	0	0	11	1	1	0	1	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEL
	6w2a	A	0	0	0	11	1	0	11	0	1	0	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEHL
	6w79	AB	1	1	0	1	0	0	1	1	1	11	11	1	11	1	1	11	0	0	0	1	1	1	0	0	0	CE
	6wco	AB	1	1	0	1	1	0	1	1	1	11	1	1	11	1	1	11	0	0	0	1	1	1	0	0	0	CE
	6xhl	A	0	0	1	11	0	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
	6xhn	A	0	0	0	1	0	0	11	1	1	11	1	21	11	11	1	11	0	0	1	0	0	11	1	1	0	CEL
	6xho	A	1	1	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
	6y7m	AB	0	1	0	11	1	0	11	1	1	11	0	21	11	10	1	11	1	1	1	1	1	1	0	0	0	CEH
SARS-CoV-2	6lu7	AB	1	1	0	1	0	0	11	1	1	11	0	21	11	11	1	11	0	1	1	0	0	11	11	1	1	CEL
	6lze	AB	0	0	0	1	1	1	11	1	1	1	1	21	11	10	1	11	0	0	1	1	1	1	0	0	0	CEH
	6m0k	AB	0	0	0	1	1	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	1	0	0	0	0	CE
	6m2n	A	0	0	0	1	1	0	0	0	1	11	0	1	0	1	1	10	0	0	0	1	0	1	0	0	0	
	6m2n	B	0	0	0	1	1	0	0	1	1	11	0	1	0	1	1	11	0	0	0	1	1	1	0	0	0	
	6w63	AB	1	1	0	1	0	0	1	1	1	11	11	1	11	1	1	11	0	0	0	1	0	1	0	0	0	CE
	6wnp	AB	0	0	0	1	0	1	0	0	1	11	1	21	0	11	1	11	1	0	0	1	1	1	1	0	1	CEL
	6wtj	AB	0	0	0	1	1	0	11	0	1	1	0	21	11	11	1	11	0	0	1	0	0	0	0	0	0	CE
	6wtk	AB	0	0	0	1	1	0	11	1	1	11	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
	6wtt	AB	0	0	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	0	11	1	1	1	CEL
	6wtt	B	0	0	0	1	0	0	0	1	1	1	1	21	11	11	1	11	0	0	1	1	0	11	1	0	1	CEL
	6xa4	AB	0	0	0	1	1	0	1	1	1	1	0	21	1	11	1	11	0	0	0	0	0	1	1	0	0	CE
	6xb1	AB	0	0	1	1	0	0	0	0	0	1	1	11	1	1	0	0	0	0	0	0	0	0	0	0	0	
	6xb2	AB	0	0	0	1	0	0	0	0	0	1	0	21	0	0	0	0	0	0	0	0	0	0	0	0	0	
	6xbg	A	0	1	0	11	1	0	11	1	1	11	0	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEHL
	6xbh	AB	0	0	0	1	1	1	11	0	1	1	0	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEHL
	6xbi	A	1	1	0	11	0	0	1	0	1	11	0	21	11	11	1	11	0	1	1	1	0	11	1	1	1	CEL
	6xch	AB	0	0	0	1	1	1	0	0	11	1	0	21	0	11	1	11	0	0	0	1	0	1	1	0	0	CEH
	6xfn	AB	0	1	0	11	0	0	1	1	1	11	11	21	11	11	0	1	0	0	0	0	0	1	0	0	0	CE
	6xhm	A	0	0	1	1	0	0	11	1	1	0	1	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEL
	6xmk	A	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
	6xoa	A	0	0	0	1	1	0	11	1	1	11	11	11	1	0	1	11	0	1	1	1	1	11	0	1	11	CEL
	6xqs	AB	0	1	0	11	1	0	0	0	1	11	0	21	0	11	1	11	1	1	0	1	1	11	1	1	1	CEHL
	6xqt	A	1	1	0	11	1	1	0	1	1	11	0	21	0	11	1	11	1	1	0	1	1	1	1	1	1	CEHL
	6xqu	AB	0	0	0	11	1	0	0	1	1	11	0	21	1	11	1	11	1	1	0	1	1	1	1	0	1	CEHL
	6xr3	AB	1	0	0	1	0	0	11	0	1	1	0	21	11	11	1	11	0	1	1	0	0	11	1	1	0	CEL
	6y2f	AB	0	1	0	11	1	0	11	1	1	11	0	21	11	11	1	11	1	1	1	1	0	1	0	0	0	CEH
	6y2g	A	0	1	0	11	1	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	0	1	0	0	0	CEH
	6ynq	AB	0	0	0	0	0	0	1	1	1	0	0	21	11	1	0	1	0	0	0	0	0	0	0	0	0	
	6yvf	AB																										
	6z2e	AB	0	1	1	1	0	0	11	0	1	11	1	21	11	11	1	11	0	0	1	0	1	11	11	1	1	CEL
	6zrt	AB	0	1	0	11	0	0	0	0	1	11	0	21	1	11	1	11	1	1	0	0	1	11	1	1	1	CEL
	6zru	AB	0	0	0	11	1	1	0	0	0	11	0	21	0	11	1	11	1	1	0	1	1	1	1	0	1	EHL
	7aku	AB	0	0	0	1	0	0	1	1	1	1	0	21	1	11	1	11	0	0	0	1	0	11	0	0	0	CE
	7b83	AB	1	1	1	21	0	0	0	0	1	0	0	21	0	0	0	0	0	0	0	0	0	0	0	0	0	R
	7bqy	AB	0	1	1	1	0	0	11	1	1	11	0	21	11	11	1	11	0	1	1	0	1	11	11	0	1	CEL
	7brp	A	0	0	0	11	1	0	0	0	11	11	0	21	0	11	1	11	0	0	0	1	0	1	1	0	1	CEHL
	7buy	AB	0	0	0	1	1	0	0	0	0	11	0	21	0	1	1	0	0	0	0	1	0	0	0	0	0	
	7c6s	AB	0	0	0	11	1	1	0	0	1	11	0	21	0	11	1	11	0	0	0	1	1	1	1	0	1	CEHL
	7c6u	AB	0	0	0	1	1	1	11	1	1	1	1	21	11	11	1	11	0	0	1	1	0	1	0	0	0	CEH
	7c7p	A	0	1	0	11	1	0	0	0	1	11	0	21	0	11	1	11	1	1	0	1	1	11	1	0	1	CEHL
	7c8b	AB	0	0	0	1	1	1	1	0	1	11	1	21	11	0	1	11	0	0	1	1	1	1	0	0	0	CEH
	7c8r	AB	1	1	1	11	0	0	11	1	1	1	1	21	11	11	1	11	1	1	1	0	1	11	1	1	1	RCEL
	7c8t	AB	0	0	0	1	1	1	11	1	1	11	1	21	11	10	1	11	1	1	1	1	1	1	1	1	1	CEHL

5c5o	A	B	1	0	0	1	1	0	1	1	1	11	0	21	11	10	0	1	0	0	0	1	0	0	0	0	0	CE
6w2a	A	B	0	0	0	1	1	0	1	0	1	1	1	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
6xhl	A	B	0	0	1	11	0	0	1	1	1	1	1	21	11	11	1	11	0	0	1	0	0	11	1	1	0	CEL
6xhn	A	B	0	0	0	1	1	0	11	1	1	11	1	21	11	11	1	11	0	1	1	0	1	11	1	1	0	CEL
6xho	A	B	1	1	0	1	0	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
6m2n	A	C	0	0	0	1	1	0	0	1	1	11	0	1	0	0	1	10	0	0	0	0	0	0	0	0	0	
6m2n	B	D	0	0	0	1	1	0	0	0	1	11	0	1	0	0	1	10	0	0	0	0	0	0	0	0	0	
6wtt	B	C	0	0	1	11	1	0	11	1	1	0	1	21	11	11	1	11	0	1	1	1	1	11	1	0	1	CEHL
6xbg	A	B	0	1	1	11	1	0	1	1	1	11	0	21	11	11	1	11	0	0	1	0	0	1	0	0	0	CEH
6xbi	A	B	1	1	0	11	0	0	1	0	1	11	1	21	11	11	1	11	0	1	1	1	0	11	1	1	1	CEL
6xhm	A	B	0	0	1	11	0	0	11	1	1	0	1	21	11	11	1	11	0	0	1	0	1	11	1	1	0	CEL
6xmk	A	B	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	1	11	1	0	0	CEL
6xoa	A	C	0	0	0	1	1	0	1	1	0	11	11	11	11	0	1	11	0	1	1	1	1	11	1	0	1	CEL
6xqt	A	B	0	1	0	11	1	1	0	1	1	11	0	21	1	11	1	11	1	1	0	1	1	1	1	1	1	CEHL
6y2g	A	B	0	1	0	11	1	0	11	1	1	11	1	21	11	11	1	11	1	1	0	1	1	0	0	0	0	CEH
7brp	A	B	0	0	0	11	1	0	0	0	11	11	0	21	0	11	1	11	0	0	0	1	1	1	1	0	1	CEHL
7c7p	A	B	1	1	0	11	0	0	0	0	0	11	1	21	0	1	0	0	0	0	0	1	1	1	0	0	0	C

7c8u	AB	0	0	0	1	1	0	11	0	1	11	0	21	11	11	1	11	0	0	1	1	0	0	0	0	0	CE
7cbt	A	0	0	0	1	0	0	11	1	1	0	1	21	11	11	1	11	0	0	1	1	1	1	0	0	0	CE
7com	A	0	0	1	11	1	0	0	0	1	11	0	21	0	11	1	11	1	1	0	1	1	11	1	0	1	CEHL
7cx9	AB	0	0	0	1	0	0	0	0	0	0	0	21	0	1	1	0	0	0	0	0	0	0	0	0	0	
7d1m	A	0	0	0	11	1	0	11	0	1	1	0	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEHL
7d1o	AB	1	1	0	11	1	1	1	1	1	11	0	21	0	11	1	11	1	1	0	1	1	1	1	1	1	CEHL
7d3i	AB	0	0	0	1	0	0	11	0	1	1	0	21	11	11	1	11	0	0	1	1	1	1	0	0	0	CE
7jkv	A	1	0	0	1	1	0	11	1	1	1	1	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEL
7joy																											
7ju7	AB	1	0	0	1	1	0	1	1	1	0	0	10	11	11	1	1	0	0	0	0	0	0	0	0	0	E
7jyc	AB	0	1	0	11	1	1	1	1	1	11	0	21	0	11	1	11	1	1	0	1	1	1	1	1	1	CEHL
7k40	AB	0	0	0	11	1	1	0	0	1	11	1	21	0	11	1	11	1	1	0	1	1	1	1	0	1	CEHL
7k6d	AB	0	1	0	11	1	0	0	0	1	11	0	21	0	11	1	11	1	1	0	0	1	11	1	1	1	CEHL
7k6e	AB	0	1	0	11	0	0	0	0	1	11	0	21	0	11	1	11	1	1	0	0	1	11	1	1	1	CEL
7khp																											
7lfp	A																										
7nev	AB	0	0	0	1	0	1	0	0	1	1	0	21	0	11	1	11	0	0	0	1	1	1	1	0	0	EL
PDBid	BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	Ligand interactions
	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker					

7c8u																										
7cbt	B	0	0	0	1	0	0	11	1	1	0	0	21	11	11	1	11	1	0	1	0	0	11	0	0	0	CE
7com	B	0	0	0	11	0	0	0	0	1	11	0	21	0	11	1	11	0	1	0	1	1	1	1	0	1	CEL
7cx9																										
7d1m	B	0	0	0	11	0	0	11	0	1	1	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
7d1o																										
7d3i																										
7jkv	B	1	0	1	1	1	0	1	0	1	1	1	21	11	11	1	11	0	0	1	0	0	11	1	1	0	CEL
7joy	B	0	0	0	11	1	0	11	1	0	11	1	11	11	11	1	11	1	1	1	1	1	11	0	1	11	CEHL
7ju7																										
7jyc																										
7k40																										
7k6d																										
7k6e																										
7khp	B	0	0	0	0	1	0	11	1	0	11	1	20	11	1	1	1	1	1	1	1	1	11	0	1	1	CEL
7lfp																										
7nev																										
PDBid	BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	Ligand interactions
	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker					

The assignments of contacts are as follows: 1 for nonpolar contact, 10 for polar contact, 11 for those containing both polar cond nonpolar contacts, 20 for covalent bond, and 21 for those containing both covalent and nonpolar contacts. Coordination between Metal ion and S or O is classified as covalent here. Polar and nonpolar contacts were assigned by LigPlot (35). Covalent bond is defined according to PyMol. MC and BC are moving cluster and binding cluster, respectively. The definition of binding mode is as follows: C: (H >= 2 and H+N >= 3) or (H+N >= 5) ; E: (H >= 2 and H+N >= 3) or (H+N >= 5) ; L: (H >= 1 and H+N >= 3) or (H+N>= 4) ; H: (H >= 1 and H+N >= 2) or (H+N>= 3); Core: (H >= 1 and H+N >= 2) or (H+N >= 3). Here H and N dinote the numbers of polar and nonpolar contacts, respectively. The enttries, 6yvf and 7lfp, bind ligands at portions of the protein other than the major binding sites, and no imformatiton is given in the table; instead the binding sites are listted here: 6yvf A:63,78,79,80,81,88,90; 7lfp A:4,5,7,125,126,127, B:5,7,127 (residue numbers without underline are for nonpolar contacts, and with underline for polar contact). The minor 16 binding sites are Thr21 (1), Thr24 (6), Asn28 (1), Pro39 (1), Cys44 (10), Thr45 (5), Ala46 (7), Asn51 (1), Tyr67 (1), Lys102 (1), Gly146 (1), Ser147 (1), Cys156 (2), Phe185 (2), Val186 (10), Ala193 (1), where the numbers of the parentheses are the number of occurrence of the contacts. The liagnd interaction in 6xoa was chosen for the interaction between chain A (donor) and chain C (acceptor), and the interaction between chain A (acceptor) and chain C (donor) was not calculated here.

Dataset S4. Summary of the ligand-bound entries supplemented to Dataset S1.

species	protein				ligand				comments	PC1					C-loop conformation								PC1					C-loop conformation								dimer		
	PDB ID	mutation	residues added to N-term	missing N-terminal residues#	name in PDB	name by authors	peptide or mimic@	Ki, IC_{50}*, EC_{50}^ (μM)		C-loop	E-loop	H-loop	Linker	Domain III	main-chain HB within 138-144	HB 138-172[&]	HB 139-126[&]	HB 140-1[&]	HB 141-118[&]	HB 143-28[&]	distance 165Cα-140Cβ	distance 165Cα-141Cβ	distance 2-214	C-loop	E-loop	H-loop	Linker	Domain III	main-chain HB within 138-144	HB 138-172[&]	HB 139-126[&]	HB 140-1[&]	HB 141-118[&]	HB 143-28[&]	distance 165Cα-140Cβ	distance 165Cα-141Cβ	distance 2-214	PC1 Domain III	PC2 Domain III	distance between two 285 Cα's
SARS-CoV	6w79				X77	X77				0.571	0.571	-1.274	1.296	6.618	141O-144N	1	1	1	1	1	7.801	11.379	7.671																0.001	6.13	8.255
	7k0g		MH6	MHHHH(-2) of A,B	B1S/K36	2	P		B1S and K36 are stereoisomers, which are not distinguished.	0.669	0.055	-1.17	-2.642	-11.425	141O-144N	1	1	0	1	1	7.309	11.083	8.611																0.001	-2.789	5.257
	7k0h		MH6	MH6 of A,B	VR4	5	P			0.482	0.914	0.238	-2.613	-5.659	141O-144N	1	1	0	1	1	7.544	11.364	7.017	0.452	0.302	-0.308	-1.268	36.635	141O-144N	1	1	0	1	1	7.437	11.284	10.048	-29.283	19.527	8.908
	7icp				UED	GC373	P			0.738	0.546	-0.203	0.41	3.343	141O-144N	1	1	0	1	1	7.463	11.246	7.255																0.001	9.125	7.831
	7icq				UED	GC373	P			0.581	0.485	-0.493	0.686	2.609	141O-144N	1	1	0	1	1	7.452	11.350	7.084																0.002	8.19	7.844
SARS-CoV-2	7a1u				FUA	Fusidic acid				0.591	-0.627	-1.131	-0.49	-4.356	141O-144N	1	1	1	1	1	7.577	11.358	6.111																-0.001	-10.207	5.014
	7abu				R6Q	RS102895		19.8^ 16.73^	R6Q is between the surface of domain III and C-loop of another protomer	1.237	-1.33	-1.399	-0.274	-6.221	141O-144N	1	1	1	1	1	7.713	11.548	6.256																0.002	-10.44	5.341
	7adw				R7Q	Dimethyl propio phenone				1.109	-0.625	-1.718	-0.25	-6.739	141O-144N	1	1	1	1	1	7.766	11.511	6.047																-0.001	-11.421	5.133
	7aeg				F2G	5	P		Q306 do not exist.	0.955	-0.188	-1.467	0.434	-9.039	141O-144N	1	1	1	1	1	7.629	11.552	6.291																-0.001	-13.825	5.250
	7aeh				R8H	1	P	3*	Q306 do not exist.	0.418	-0.594	-1.089	-1.314	-1.344	141O-144N	1	1	1	1	1	8.140	11.656	6.561																-0.001	-6.262	5.139
	7af0				R9W	Ipidacrine			R9W is a small compound located on the surface of domain III.	1.061	-0.879	-1.829	0.017	-8.358	141O-144N	1	1	1	1	1	7.823	11.672	6.235																0	-11.839	5.140
	7aga				LZE	AT7519		25.16 43.95^	LZE is at the interface of domain II and III.	0.969	-1.09	-1.071	-0.484	-5.861	141O-144N	1	1	1	1	1	7.544	11.335	6.146																-0.001	-10.886	5.358
	7aha				SIN	Maleate				1.063	-1.29	-1.728	-0.321	-8.223	141O-144N	1	1	1	1	1	7.673	11.530	5.956																0.001	-11.482	5.239
	7ak4				CB1	Tretazicar				1.04	-0.522	-1.629	0.031	-5.522	141O-144N	1	1	1	1	1	7.332	11.049	6.125																-0.001	-11.268	5.125
	7amj				RMZ	PD 168568			RMZ is between the surface of domain III and C-loop of another protomer.	1.162	-1.085	-1.617	-0.246	-7.536	141O-144N	1	1	1	1	1	7.631	11.463	6.034																0	-11.772	5.151
	7ans				RNW	Adrafinil				0.802	-0.585	-1.548	-0.19	-5.445	141O-144N	1	1	1	1	1	7.779	11.528	6.312																0	-8.487	5.130
	7aol	N72L			RQH	Climbazole			RQH is a small compound located on the molecular surface.	1.044	-1.006	-1.725	0.004	-7.533	141O-144N	1	1	1	1	1	7.730	11.627	6.063																0	-11.516	5.186
	7ap6				RQN	MUT056399		38.24 36.73^	M49(Alt B) and M65 clashes with RQH.	0.848	-0.488	-2.251	-0.06	-5.364	141O-144N	1	1	1	1	1	7.701	11.436	6.341																-0.002	-8.891	5.163
	7aph				RT2	Tofogliflozin			RT2 is on the surface of domain III.	0.858	-0.492	-1.66	-0.163	-6.477	141O-144N	1	1	1	1	1	7.430	11.643	5.859																0	-11.15	5.275
	7aqe				RV5	UNC-2327				0.76	-1.062	-1.56	-0.4	-6.909	141O-144N	1	1	1	1	1	7.807	11.574	6.499																0.002	-10.237	5.080
	7aqi				QEL	Ifenprodil			QEL is on the surface of domain III.	1.141	-0.966	-1.791	-0.09	-7.78	141O-144N	1	1	1	1	1	7.826	11.614	6.055																0.001	-10.521	5.117
	7aqj				S7H,RV8	Triglycidyl isocyanurate		30.02^ 31.51^	S7H and RV8 are stereoisomers. The epoxide group of RV8 is eliminated to make alcohol of S7H.	0.571	-1.096	-1.731	-0.155	-6.182	141O-144N	1	1	1	1	1	7.325	11.269	6.302																0.001	-7.911	5.411
	7arf				RVW	thioglucose			RVW is a small compound located on the molecular surface. C145 is di-oxydized to be CSD (3-sulfinoalanine).	1.082	-1.854	-1.093	-0.906	-5.948	141O-144N	1	1	1	1	1	7.778	11.647	6.374																0	-9.718	5.365
	7avd_B				S1W	SEN1269			Chain A is ligand-unbound.													0.928	-1.453	-2.084	-4.254	-3.084	141O-144N	1	1	1	1	1	7.210	11.149	6.641	-6.19	-9.655	5.526
	7awr				S7W	Tegafur			S7W is a small compound located on the molecular surface.	0.984	-0.964	-1.436	-0.363	-6.332	141O-144N	1	1	1	1	1	7.778	11.616	6.413																0	-11.495	5.142
	7aws				S8E	TH-302				1.249	-0.99	-1.743	-0.032	-7.853	141O-144N	1	1	1	1	1	7.812	11.594	6.121																0.001	-11.281	5.338
	7awu				S8B	LSN2463359			Cys145 is mono-oxydized to be CSO (hydroxycysteine). N142(Alt A) and M165(Alt A) clashes with S8B.	0.959	-0.781	-1.683	-0.112	-5.146	141O-144N	1	1	1	1	1	7.740	11.475	6.137																-0.001	-8.529	5.272
	7aww				CLU	Clonidine			CLU is a small compound located on the molecular surface.	1.091	-1.031	-1.812	-0.129	-6.623	141O-144N	1	1	1	1	1	7.799	11.737	6.444																0	-10.695	5.113
	7ax6				S8H	Glutathione isopropyl ester	P		S8H is a small compound located on the molecular surface.	1.124	-0.824	-2.058	0.206	-5.323	141O-144N	1	1	1	1	1	7.604	11.278	6.271																0	-7.787	5.369
	7axm				93J	Pelitinib		1.25^ 1.24^	93J is between the surface of domain III and C-loop of another protomer.	0.908	-0.638	-1.607	-0.182	-7.143	141O-144N	1	1	1	1	1	7.781	11.551	6.310																-0.001	-10.848	5.186
	7axo				QCP	AR-42			QCP is on the surface of domain III.	1.067	-1.034	-1.649	-0.081	-8.229	141O-144N	1	1	1	1	1	7.730	11.583	6.279																0	-11.13	5.305
	7ay7				S8T	Isofloxythepin		4.8 4.92^	S8T is double configurations.	1.035	-1.305	-1.69	-0.514	-7.277	141O-144N	1	1	1	1	1	7.733	11.598	6.065																-0.001	-10.844	5.237
	7b3e				MYC	myricetin				0.242	0.123	-0.022	0.768	4.312	141O-144N	1	1	1	1	1	7.830	11.660	7.348	0.49	0.07	0.336	1.034	-1.446	141O-144N	1	1	1	1	1	7.735	11.620	6.953	0.553	2.512	5.801
	7bak				Se	ebselen		0.670* 4.67^	Only Se is modeled.	0.917	-2.287	-1.024	-2.079	-4.729	141O-144N	1	1	1	1	1	7.456	11.651	6.271																-0.001	-8.554	5.263
	7bal				Se	MR6-31-2		0.824* 1.78^	Only Se is modeled.	0.614	-2.121	-1.137	-2.421	-4.218	141O-144N	1	1	1	1	1	7.658	11.922	6.163																0.001	-8.751	5.431
	7be7				ALD	MG-132	P			0.809	0.816	0.264	1.484	0.619	141O-144N	1	1	1	1	1	7.765	11.495	6.668	1.017	0.677	0.418	1.447	-3.208	141O-144N	1	1	1	1	1	7.643	11.526	6.667	-3.594	-2.657	5.429
	7bfb				9JT	ebselen			There are five 9JT's (3 in chain A and 2 in chain B). Only a fragments of 9JT is modeled. Se-C145 is only in chain A.	0.551	-0.644	-0.781	0.9	5.914	141O-144N	1	1	1	1	1	7.642	11.455	7.639	0.622	-0.188	0.424	1.601	-6.68	141O-144N	1	1	1	1	1	7.809	11.748	6.743	4.273	2.502	5.781
	7bgp				ALD	MG-132	P			0.753	0.75	0.017	1.367	0.675	141O-144N	1	1	1	1	1	7.808	11.525	6.778	0.975	0.719	0.215	1.426	-2.979	141O-144N	1	1	1	1	1	7.652	11.511	6.674	-3.239	-1.784	5.501
	7ca8_A			SG of A,B	FNO	Shikonin			Chain B is ligand-free. C-terminal residues 299-306 do not exist.	-1.166	-0.394	-0.02	1.159	6.198		1	0	0	0	1	8.472	13.067																	1.22	12.886	8.610
	7cb7		GSGGG	GSGGG	B1S,K36	GC376	P	0.89*	B1S,K36 are stereoisomers and are not distinguished.	0.967	0.307	1.304	-2.675	-8.466	141O-144N	1	1	0	1	1	7.214	10.835	9.220	0.509	1.402	0.868	0.532	27.909	141O-144N	0	1	0	1	1	7.391	11.095	9.652	-27.704	10.327	6.850
	7cut				Z-VAD-FMK	Z-VAD-FMK	P	0.59*		0.401	0.141	-0.474	2.059	-8.934	141O-144N	1	1	1	1	1	7.758	11.545	6.730																-0.001	-10.874	5.124
	7cuu				ALD	MG-132	P	3.91*		0.938	0.968	-1.588	-0.103	-9.252	141O-144N	1	1	1	1	1	7.451	11.158	6.033	1.248	0.706	-0.33	0.517	-9.227	141O-144N	1	1	1	1	1	7.474	11.145	6.255	2.951	-9.454	5.502
	7dk1				Zn	Zn		0.3251*	Three Zn exist (two at C145 and C156 of chain A and one at C145 of chain B).	0.739	0.2	-0.157	0.362	-6.124	141O-144N	1	1	1	1	1	7.670	11.425	6.857	0.648	0.276	-0.416	0.257	-3.16	141O-144N	1	1	1	1	1	7.676	11.466	6.566	-2.964	-6.957	5.296
	7dpp				MYC	Myricetin		0.63*	302-306 do not exist	0.09	0.753	18.39	1.63	-4.801	141O-144N	1	1	1	1	1	7.721	11.723	6.592																0	-7.419	5.228
	7dpu				HER	3		0.30*		-3.132	-2.594	-0.605	-1.758	2.383	140O-143N	0	0	0	0	0	14.007	12.403	6.450	0.461	-2.473	-1.09	-2.557	-2.87	141O-144N	1	1	1	1	1	7.291	11.557	6.402	1.948	-0.731	5.830
	7dpv_AC				HF0	7		0.26*	Tetramer (two asymmetric dimers).	0.294	-0.261	0.74	-0.04	4.338	141O-144N	1	1	1	1	1	7.845	11.669	7.249	-0.172	-0.454	0.072	1.088	-5.247	141O-144N	0	1	0	0	1	7.326	12.125	6.577	3.38	0.051	5.968
	7dpv_BD				HF0	7		0.26*		0.263	-0.203	0.925	-0.241	4.505	141O-144N	1	1	1	1	1	7.768	11.734	7.551	-0.152	-1.023	0.506	0.99	-19.187	141O-144N	0	1	0	0	1	7.375	11.987	6.451	12.614	-12.208	5.882
	7e18				HUR	YH-53	P	0.0347		0.142	1.494	0.476	-3.419	-4.251	141O-144N	1	1	1	1	1	7.540	11.413	6.358																0	-11.317	5.021
	7e19				HUO	SH-5	P	0.0145		0.665	2.883	-1.023	-0.635	-4.288	141O-144N	1	1	1	1	1	7.453	11.253	6.358																0.001	-8.024	5.516
	7ein				PRD_000216	Leupeptin	P			0.917	0.696	-0.461	-2.025	-12.461	141O-144N	1	1	1	1	1	7.438	11.454	6.609	1.021	0.622	-0.447	-1.977	-12.935	141O-144N	1	1	1	1	1	7.406	11.402	6.686	0.245	-13.643	5.297
	7fay				2XI	(R)-1a				0.31	-0.519	-1.852	-1.004	-5.241	141O-144N	1	1	1	1	1	7.549	11.215	6.625																0.001	-9.36	5.421
	7faz				2RI	Y180				0.362	-0.333	0.046	1.413	-1.841	141O-144N	1	1	1	1	1	7.663	11.225	6.692	0.415	-0.563	0.296	-0.655	-3.518	141O-144N	1	1	1	1	1	7.657	11.277	6.814	-3.362	-5.279	5.175
	7jpz				GHX	MPI1	P	0.0979* 0.100^	Cys128 and Cys300 are mono-oxydized to be CSO (hydroxycysteine).	0.845	-2.031	-1.243	-2.54	-6.463	141O-144N	1	1	1	1	1	7.272	11.287	6.236																-0.001	-9.468	5.392
	7jq0				VHV	MPI3	P	0.0083 0.0085^	Cys128 and Cys300 are mono-oxydized to be CSO (hydroxycysteine).	1.244	0.71	-0.893	-2.235	-7.62	141O-144N	1	1	1	1	1	7.378	11.167	6.225																-0.001	-11.455	5.545
	7jq1				VHJ	MPI4	P	0.0147 0.015^	Cys128 and Cys300 are mono-oxydized to be CSO (hydroxycysteine).	0.87	0.283	-0.626	-1.755	-7.181	141O-144N	1	1	1	1	1	7.393	11.308	6.446																-0.002	-10.807	5.370
	7jq2				VHM	MPI5	P	0.0322 0.033^	Cys128 is mono-oxydized to be CSO (hydroxycysteine).	0.937	0.088	-1.051	-2.408	-7.104	141O-144N	1	1	1	1	1	7.395	11.199	6.370																0	-10.158	5.364
	7jq3				VHP	MPI6	P	0.0586 0.060^	Cys128 and Cys300 are mono-oxydized to be CSO (hydroxycysteine).	0.988	-0.111	-0.925	-1.313	-7.336	141O-144N	1	1	1	1	1	7.348	11.339	6.377																0	-10.078	5.278
	7jq4				XM2	MPI7	P	0.0459 0.047^	Cys128 and Cys300 are mono-oxydized to be CSO (hydroxycysteine).	0.99	-0.538	-0.844	-1.791	-8.135	141O-144N	1	1	1	1	1	7.427	11.390	6.365																-0.001	-10.182	5.286
	7jq5				NOL	MPI8	P	0.1026 0.105^	Cys128 and Cys300 are mono-oxydized to be CSO (hydroxycysteine).	0.949	0.04	-0.735	-1.583	-8.522	141O-144N	1	1	1	1	1	7.456	11.379	6.142																0.001	-10.749	5.249

7jsu				UED	GC376	P			1.047	0.879	-0.052	-0.719	-9.114	141O-144N	1	1	1	1	1	7.342	11.097	6.291															0.001	-11.418	5.785
7jt0				LW1	MAC-5576			Chloropxypyridine in MAC-5576 is reduced to be LW1.	0.481	1.061	3.173	1.267	-6.907	141O-144N	1	1	1	1	1	7.430	11.494	6.350															0	-9.118	5.605
7jt7				TG3	4	P			0.601	1.57	-0.764	0.948	1.359	141O-144N	1	1	1	1	1	7.428	11.100	6.915															0.001	-2.831	5.596
7jw8_AB				TG3	4	P		Tetramer (two hheterodimers). Space group of P1.	0.802	1.708	-0.829	0.198	2.182	141O-144N	1	1	1	1	1	7.338	11.067	6.892	0.734	1.531	-0.397	0.687	-0.389	141O-144N	1	1	1	1	1	7.450	11.117	6.398	-2.082	-3.243	5.641
7jw8_CD				TG3	4	P			0.886	1.597	-0.47	0.756	-3.862	141O-144N	1	1	1	1	1	7.355	11.087	6.184	0.825	1.973	-0.717	0.645	2.03	141O-144N	1	1	1	1	1	7.324	11.025	6.669	-0.69	-4.698	5.655
7k0e		SNIG	SNIGS of A,SNIGSGFR of B	K36	2	P	0.18* 0.086[+] 0.069[+]		0.563	0.438	0.591	-2.568	-11.146	141O-144N	1	1	0	1	1	7.247	10.863	6.348	0.635	0.715	0.188	-1.155	33.482	141O-144N	1	1	0	1	1	7.438	11.131		-31.224	13.284	7.820
7k0f		SNIG	SNIGSGF of A and B	VR4	5	P	1.31*		0.607	0.834	0.318	-2.659	-14.107	141O-144N	1	1	0	1	1	7.599	11.283		0.339	0.334	0.546	-1.668	39.172	141O-144N	1	1	0	1	1	7.377	11.222		-36.973	15.988	8.009
7kvl_A		GAM		X4P	FMAX E01			X4P is a small compound located on the surface of domain III.	-2.274	-0.545	0.161	1.481	9.464		1	0	0	1	0	13.961	8.949	10.162															-4.725	19.553	10.009
7kvr_B		GAM	GAM of A, GAMS of B	XV4	FMAX E09			XV4 is a small compound located on the surface of domain III.															-1.509	0.119	2.26	1.815	7.42		1	0	0	0	1	10.777	11.892	7.958	-2.043	13.813	9.542
7kx5				X7V	Jun8-76-3A			1-oxybenzotriazole in X7V is replaced by C145.	0.797	-0.994	-1.472	0.267	-10.026	141O-144N	1	1	1	1	1	7.336	11.178	6.010															0.001	-16.056	4.840
7kyu				XC4	1H-indole-5-carboxylate				0.405	0.65	0.517	1.693	-6.392	141O-144N	1	1	1	1	1	7.717	11.485	6.643															0.001	-10.877	5.351
7l0d				0EN	ML188		2.5*		0.591	-0.913	-1.61	-0.719	-8.738	141O-144N	1	1	1	1	1	7.736	11.540	6.218															0.001	-12.377	5.134
7l10				XEY	4				0.621	-0.484	1.411	1.861	-4.572	141O-144N	1	1	1	1	1	7.868	11.729	6.521															0.002	-7.194	5.317
7l11				XF1	5		2.5[+] 1.5[+]		0.434	-0.35	-1.164	0.484	4.795	141O-144N	1	1	1	1	1	7.941	11.709	7.440	0.607	-0.127	0.658	-0.748	3.526	141O-144N	1	1	1	1	1	7.947	11.671	6.894	-3.581	2.524	5.903
7l12				XF4	14		3.2[+]		0.329	-1.203	-0.984	-1.702	-2.678	141O-144N	1	1	1	1	1	7.839	11.504	6.588															0	-6.177	5.152
7l13_A				XF7	21		11.3[+]	Chain B is ligand-unbound.	0.749	-1.485	-0.377	-0.409	1.567	141O-144N	1	1	1	1	1	7.731	11.369	7.493															4.833	-1.553	5.504
7l14				XFD	26		2.0[+] 0.98[+]		0.524	0.429	-1.199	1.401	4.677	141O-144N	1	1	1	1	1	8.001	11.788	7.218	0.665	0.118	0.603	1.408	-1.426	141O-144N	1	1	1	1	1	7.930	11.675	6.835	-0.38	0.494	5.480
7l5d				XNJ	demethylated analog of masitinib				0.384	0.236	-0.304	1.924	-8.086	141O-144N	1	1	1	1	1	7.725	11.260	6.430															0	-12.961	5.177
7lb7				PRD_002448	Telaprevir	P		Neutron diffraction determining the H positions.	0.679	0.387	-0.173	-1.419	-0.27	141O-144N	1	1	1	1	1	7.814	11.342	6.698															0	-3.815	5.913
7lbn				PRD_002460	Calpain I	P			0.968	0.371	-0.416	2.009	-9.944	141O-144N	1	1	1	1	1	7.507	11.246	6.202															0.001	-12.738	5.370
7lco				XTJ	1i	P	0.14* 1.1[+]		1.163	0.157	-0.723	-2.727	-9.175	141O-144N	1	1	1	1	1	7.227	10.940	6.217															0	-11.315	5.341
7lcs				XTP	1a	P	0.05* 1.1[+]		0.962	0.283	-1.216	-2.999	-10.364	141O-144N	1	1	1	1	1	7.382	11.064	6.234															0.001	-12.38	5.372
7lct				XU4	1g	P	0.27 1.1[+]		0.997	1.708	-0.469	-3.472	-2.16	141O-144N	1	1	1	1	1	7.206	10.920	6.488															-0.001	-6.006	5.892
7ldl				XV4	1f	P	0.06* 0.9[+]		0.836	0.717	1.008	-2.714	-5.606	141O-144N	1	1	1	1	1	7.783	11.605	6.612	0.805	1.098	0.497	-2.757	-4.067	141O-144N	1	1	1	1	1	7.774	11.674	6.551	-1.203	-8.473	5.407
7ldx		GAM	GAM of B	R9V	F2X E06			Small ligand R9V is on the interfavcce between domain I and III.	0.25	-0.703	0.217	0.799	9.302		0	0	0	0	1	8.955	12.568	10.136	-10.835	1.098	2.185	2.142	14.339	139O-142N 140O-143N	0	0	0	0	0	9.885	14.054	7.643	-4.945	18.997	9.873
7lfe_A		GAM		XWS	F2X E03			Chain B is ligand-unbound.	-2.869	-0.476	0.038	1.181	9.482		0	0	0	0	0	13.092	11.059	10.211															-2.15	17.03	9.750
7lkr		SNIG	SNIGSGFR of A, SNIGSGF of B	Y91,Y8Y	2a	P	0.18*	Stereoisomers, Y91,Y8Y, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.565	0.288	0.801	-2.534	-12.944	141O-144N	1	1	0	1	1	7.307	10.868		0.588	0.628	0.363	-2.218	36.895	141O-144N	1	1	0	1	1	7.469	11.274		-35.029	16.177	7.912
7lks		SNIG	SNIGSG of A, SNIGSG of B	Y4P,Y7G	2f	P	0.14*	Stereoisomers, Y4P,Y7G, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.359	0.726	0.509	-3.016	-13.803	141O-144N	1	1	0	1	1	7.303	10.872		0.309	0.212	-0.067	-2.441	38.365	141O-144N	1	1	0	1	1	7.497	11.469		-34.904	16.69	7.806
7lkt		SNIG	SNIGSGF of A, SNIGS of B	Y4V,Y7M	2k	P	0.18*	Stereoisomers, Y4V and Y7M, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.763	0.908	1.042	-3.165	-11.059	141O-144N	1	1	0	1	1	7.370	10.958		0.736	0.447	-0.206	-2.878	34.199	141O-144N	1	1	0	1	1	7.554	11.405	9.509	-31.798	14.154	7.904
7lku		SNIG	SNIG of A, SNIGSG of B	Y91,Y8Y,Y5S,Y4D	3b	P	0.29*	Stereoisomers, Y91,Y8Y,Y5S,Y4D, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.605	0.378	0.639	-2.385	-16.332	141O-144N	1	1	0	1	1	7.303	10.866	6.574	0.669	0.53	0.362	-2.081	37.893	141O-144N	1	1	0	1	1	7.623	11.523		-37.685	13.315	8.003
7lkv		SNIG	SNIGS of A, SNIGSGF of B	Y64,Y4J	3c	P	0.26*	Stereoisomers, Y64,Y4J, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.616	0.342	1.186	-2.436	-13.375	141O-144N	1	1	0	1	1	7.305	10.949	6.359	0.71	0.997	0.354	-0.917	36.859	141O-144N	1	1	0	1	1	7.356	11.149		-36.105	15.418	7.996
7lkw		SNIG	SNIGSGF of A, SNIGSG of B	Y8V,Y8S	3d	P	0.30*	Stereoisomers, Y8V,Y8S, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.74	0.99	-0.03	-2.818	-14.148	141O-144N	1	1	0	1	1	7.316	10.890		0.698	0.47	0.305	-1.994	38.813	141O-144N	1	1	0	1	1	7.382	11.251		-37.541	14.396	8.083
7lkx		SNIG	SNIGSGFR of A, SNIGSG of B	Y71,Y51	3e	P	0.28*	Stereoisomers, Y71,Y51, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.548	0.785	0.466	-2.783	-12.755	141O-144N	1	1	0	1	1	7.318	10.921		0.614	0.567	0.42	-2.08	35.954	141O-144N	1	1	0	1	1	7.516	11.392		-34.262	14.856	7.683
7lmc_AB	C145A				C-term of chain C & C-term of Nsp4C	P		Two heterodimers. Chain A binds the C-terminus of chain C in the asymmetric unit. Chain B binds 6 residue peptide of C-term of Nsp4C.	0.809	0.43	-0.219	2.103	-7.777	141O-144N	1	1	1	1	1	7.430	10.876	7.038	0.466	0.037	-0.436	0.243	1.542	141O-144N	1	1	1	1	1	7.950	11.597	6.375	-9.102	-4.462	6.047
7lmc_CD	C145A				C-term of chain C & C-term of Nsp4C	P		Two heterodimers. Chain C binds the C-terminus of chain C in the asymmetric unit. Chain D binds 6 residue peptide of C-term of Nsp4C.	0.737	1.462	-0.696	2.203	-5.224	141O-144N	0	1	1	1	1	7.619	10.761	7.501	0.999	-0.65	-0.925	-0.264	2.282	141O-144N	1	1	1	1	1	7.309	10.478	6.550	-6.236	-0.369	6.162
7ltj				YD1	Mcule-5948770040				0.58	-0.3	-0.245	-1.19	-4.082	141O-144N	1	1	1	1	1	7.717	11.533	6.586															0	-6.481	5.433
7lyh				YHJ	UAWJ9-36-1	P			1.294	1.305	-1.032	-2.567	-11.197	141O-144N	1	1	1	1	1	7.147	10.906	6.320															0	-11.225	5.191
7lyi		HM	HMS	YHI	UAWJ9-36-3	P			1.367	-0.737	0.397	-2.077	-10.371	141O-144N	1	1	0	1	1	7.439	11.148	6.573															0	-6.746	5.567
7lzt		SNIG	SNIGS	YN1,YMY	8b	P			1.223	0.895	-1.006	-3.284	-15.355	141O-144N	1	1	0	1	1	7.250	10.915	6.523															0	-13.084	5.221
7lzu		SNIG	SNIGSGFR of A,SNIGSG of B	YKP,YKM	12b	P		Stereoisomers,YKP,YKM, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.714	0.6	0.52	-2.903	-12.141	141O-144N	1	1	0	1	1	7.394	10.976		0.454	0.287	0.329	-2.847	35.032	141O-144N	1	1	0	1	1	7.438	11.315		-33.345	15.233	7.233
7lzv		SNIG	SNIGSGF of A,B	YLS,YLM	19b	P		Stereoisomers,YLS,YLM, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.667	0.48	0.515	-2.602	-12.916	141O-144N	1	1	0	1	1	7.321	10.891		0.531	0.372	0.408	-1.704	37.87	141O-144N	1	1	0	1	1	7.414	11.159		-35.73	17.323	8.148
7lzw		SNIG	SNIGSGF of A,B	YLS,YLM	20b	P		20b is deuterated 19b. Stereoisomers,YLS,YLM, are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.634	0.326	0.661	-2.4	-15.848	141O-144N	1	1	0	1	1	7.254	10.871		0.743	0.419	0.352	-1.417	36.482	141O-144N	1	1	0	1	1	7.319	10.906		-36.529	13.83	8.303
7lzx		SNIG	SNIGSG of A,SNIG of B	YMD,YMG	1c	P		Stereoisomers,YMD,YMG,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.684	0.886	0.609	-2.502	-14.361	141O-144N	1	1	0	1	1	7.294	10.962		0.683	0.726	0.329	-2.183	41.125	141O-144N	1	1	0	1	1	7.340	11.047	9.617	-37.902	18.769	8.896
7lzy		SNIG	SNIGSG	YMM,YMJ	3c	P		Stereoisomers,YMM,YMJ,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.908	1.108	-1.013	-3.548	-12.805	141O-144N	1	1	0	1	1	7.455	11.150																-0.001	-12.817	5.317
7lzz		SNIG	SNIGSG	YMV,YMS	5c	P		Stereoisomers,YKY,YL7,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.856	1.09	-1.007	-3.447	-13.016	141O-144N	1	1	0	1	1	7.411	11.178																0.001	-14.511	5.057
7m00		SNIG	SNIGSG of A,B	YKD,YKA	13c	P		Stereoisomers,YKD,YKA,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.67	0.978	-0.594	-3.168	-11.175	141O-144N	1	1	0	1	1	7.473	11.246		0.56	1.021	-0.625	-3.21	-11.013	141O-144N	1	1	0	1	1	7.494	11.239		0.26	-13.417	5.276
7m01		SNIG	SNIGSGF of A,SNIGSG of B	YKS,YKV	14c	P		Stereoisomers,YKS,YKV,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.701	0.716	0.215	-2.854	-13.576	141O-144N	1	1	0	1	1	7.299	10.911		0.496	0.57	0.362	-2.23	33.27	141O-144N	1	1	0	1	1	7.504	11.301		-33.242	12.345	7.179
7m02		SNIG	SNIGSGF of A,SNIGSG of B	YKY,YL7	17c	P		Stereoisomers,YM1,YLV,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.511	0.709	0.506	-2.936	-14.387	141O-144N	1	1	0	1	1	7.217	10.814		0.436	0.629	-0.059	-2.73	36.926	141O-144N	1	1	0	1	1	7.491	11.382		-34.551	14.718	7.625

7m03		SNIG	SNIGSGF of A,SNIGSG of B	YLJ,YLD	18c	P		Stereoisomers,YLJ,YLD,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.625	0.442	0.904	-2.658	-14.17	141O-144N	1	1	0	1	1	7.301	10.782		0.56	0.511	-0.044	-1.788	36.999	141O-144N	1	1	0	1	1	7.455	11.204		-34.84	15.003	8.017
7m04		SNIG	SNIGS of A,SNIGSG of B	YM1,YLV	21c	P		Stereoisomers,YM1,YLV,are not distinguished. Sulfoxide of the ligand is replaced by Sg of C145. Q306 does not exist.	0.69	0.742	-0.098	-2.787	-14.142	141O-144N	1	1	0	1	1	7.377	11.055	6.642	0.537	0.644	0.367	-1.964	36.463	141O-144N	1	1	0	1	1	7.569	11.390		-35.454	15.682	7.784
7m8m_A				YSG	11		0.120*	Chain B is ligand-unbound.	0.6	-0.028	0.053	1.224	1.802	141O-144N	1	1	1	1	1	7.694	11.292	7.057														4.404	-2.185	5.293
7m8n				YSP	16		0.1*		0.809	-1.17	-0.978	-0.656	1.646	141O-144N	1	1	1	1	1	7.607	11.102	7.228	0.771	-1.094	0.478	-0.305	-1.808	141O-144N	1	1	1	1	1	7.741	11.332	6.939	-0.966	0.343	5.626
7m8o_A				YSM	19		0.037*	Chain B is ligand-unbound.	0.296	-0.987	-0.311	-1.033	3.126	141O-144N	1	1	1	1	1	7.650	11.282	7.548														4.64	-3.14	5.541
7m8p_A				YSJ	23		0.020*	Chain B is ligand-unbound.	0.62	-1.622	-0.059	0.506	1.925	141O-144N	1	1	1	1	1	7.566	11.255	7.581														1.054	-0.663	5.795
7m8x				YTJ	6		0.47*		0.42	-0.576	4.787	-0.452	-4.038	141O-144N	1	1	1	1	1	7.962	11.892	6.679														-0.001	-7.524	5.172
7m8y				YTM	15		0.110*		0.439	-1.013	-1.348	0.032	-2.055	141O-144N	1	1	1	1	1	7.715	11.292	6.755														0.001	-5.486	5.270
7m8z				YTV	29		0.25-0.50*		0.569	0.178	4.584	0.874	-3.911	141O-144N	1	1	1	1	1	7.633	11.205	6.710														0	-6.899	5.351
7m90				YTS	5O		0.25-0.50*		0.436	0.51	1.331	1.115	0.464	141O-144N	1	1	1	1	1	7.849	11.537	6.923														0.001	-3.391	5.535
7m91				YU4	2S		0.025*		0.791	-0.342	1.347	1.015	-5.03	141O-144N	1	1	1	1	1	7.754	11.448	6.649														0.001	-7.138	5.542
7mbi_AD				YWJ	15I	P	0.019* 0.30	Tetramer (two heterodimers). Trimethylpyridine-3-carboxylate of 15I is replaced by Sg of C145 to be YWJ.	0.63	0.822	0.23	-3.042	-10.168	141O-144N	1	1	1	1	1	7.495	11.153	6.425	0.28	1.578	-1.047	-3.152	0.995	141O-144N	1	1	1	1	1	7.503	11.331	6.436	-9.862	-5.929	5.809
7mbi_BC				YWJ	15I	P	0.019* 0.30'		0.336	1.906	2.801	-2.882	-3.082	141O-144N	1	1	1	1	1	7.473	11.116	6.413	0.497	1.277	0.344	-3.586	-0.519	141O-144N	1	1	1	1	1	7.380	11.099	6.565	2.081	-0.319	5.818
7mgr	C145A			AVKLQNNE	nsp8/9 substrate peptide	P		The substrate is C-term 5res of Nsp8 and N-term 4res of Nsp9, AVKLQNNEL; the last L is missing.	0.605	-0.181	-0.037	-1.321	-10.396	141O-144N	1	1	1	1	1	7.282	10.685	6.460														0.001	-12.234	5.648
7mgs	C145A			SAVLQSGF	N-term auto-processing substrate	P		The substrate is the C-terminal 8res peptide of Nsp4C, SAVLQSGF	0.965	1.489	-0.624	0.594	-9.242	141O-144N	1	1	1	1	1	7.325	10.988	6.529														0.001	-8.894	5.994
7mng				ZL7	VBY-825	P		ZL7 contains two models.	0.651	-1.598	-1.33	-3.353	-6.069	141O-144N	1	1	1	1	1	7.666	11.681	6.118														-0.001	-10.642	5.217
7mpb				ASC	Ascorbate			After Q306, GPHHHHHH is added.	0.857	-1.766	-1.173	-2.607	-8.102	141O-144N	1	1	1	1	1	7.780	11.750	6.620	0.756	-0.892	-0.4	0.158	0.552	141O-144N	1	1	1	1	1	7.507	11.469	6.692	-8.769	-6.705	5.730
7mrr				PRD_000216	Leupeptin	P			0.875	0.202	-0.849	-0.781	-13.296	141O-144N	1	1	1	1	1	7.492	11.737	6.362														0.001	-15.511	5.223
7n44				06I	13		0.042*		0.384	-1.078	3.139	-2.401	-1.979	141O-144N	1	1	1	1	1	7.947	11.577	6.601														0	-5.446	5.482
7n6n	C145S	GAMSAVLQ	GAMSAVLQ	GAMSAVLQ	N-terminal & C-terminal substrates	P		Chain A binds SAVLQ, N-terminal of Nsp4C. Chain B binds C-terminus of chain A in another unit. GAM of GAMSAVLQ (C-term of Nsp4C) is missing.	0.406	0.359	-1.893	-1.729	-5.065	141O-144N	1	1	1	1	1	7.520	11.045	6.469	1.189	0.047	0.248	2.267	-11.621	141O-144N	1	1	1	1	1	7.527	10.922	8.912	10.819	-4.564	6.120
7n89	C145A			SAVLQSGF	substrate	P		The termials of the substrate are caped by ACE and NH2, respectively.	0.88	0.23	-1.096	-2.482	-14.168	141O-144N	1	1	1	1	1	7.349	10.873	6.438	0.953	0.291	-0.878	-0.942	-9.839	141O-144N	1	1	1	1	1	7.323	10.859	6.606	-3.043	-11.271	5.525
7n8c				YD1	Mcule5948770040				0.544	-0.291	-0.369	-1.34	-3.793	141O-144N	1	1	1	1	1	7.736	11.563	6.807														-0.001	-5.717	5.508
7nbr				PRD_002382	Boceprevir	P			1.076	1.73	-0.473	-0.867	-12.363	141O-144N	1	1	1	1	1	7.527	11.487	6.397														0	-15.196	5.234
7nbs				SV6	Telaprevir	P			0.779	0.308	-0.269	-1.2	-2.199	141O-144N	1	1	1	1	1	7.572	11.365	6.511														0.001	-5.504	5.746
7nbv[4]				U88	SU3327			Four U88 per protomer bind to four distinct sites, respectively.	0.578	0.647	-0.285	1.104	5.446	141O-144N	1	1	1	1	1	7.512	11.466	7.470	0.879	0.582	13.875	1.155	-4.962	141O-144N	1	1	1	1	1	7.524	11.407	6.943	3.622	1.667	5.753
7nf5				ALD	MG-132	P			0.949	0.439	0.063	-0.209	-1.309	141O-144N	1	1	1	1	1	7.440	11.139	6.254														-0.001	-4.845	5.895
7ng3				ALD	MG-132	P			1.23	1.465	-1.032	0.698	-9.441	141O-144N	1	1	1	1	1	7.452	11.137	6.359	1.004	1.544	-0.734	-0.242	-8.807	141O-144N	1	1	1	1	1	7.447	11.201	6.065	-3.513	-9.065	5.697
7ng6				ALD	MG-132	P			1.276	1.587	-0.999	0.686	-11.172	141O-144N	1	1	1	1	1	7.420	11.193	6.350	0.987	1.661	-0.537	-0.177	-11.629	141O-144N	1	1	1	1	1	7.423	11.263	6.035	-2.057	-10.498	5.358
7nt1_B				UQW	II-F10		139.10*	Chain A is ligand-free.													0.828	-0.424	-0.469	0.009	3.753	141O-144N	1	1	1	1	1	7.718	11.478	7.578	-5.269	1.449	5.668
7nt2_B				URK	II-G11		9.39*	Chain A is ligand-free.													0.702	-0.361	-0.751	0.641	5.594	141O-144N	1	1	1	1	1	7.656	11.482	7.585	-5.61	2.08	5.805
7nt3_B				UQZ	F3		>> 1000*	Chain A is ligand-free.													0.841	-0.528	-0.406	-0.418	4.253	141O-144N	1	1	1	1	1	7.677	11.425	7.842	-4.666	1.96	5.644
7ntv_B				US8	F2		2.36*	Chain A is ligand-free.													0.623	-0.145	-0.556	0.465	6.113	141O-144N	1	1	1	1	1	7.770	11.552	7.595	-4.559	1.334	5.772
7nuk_B				USH	F1	P	3.96*	Chain A is ligand-free.													0.702	-0.11	-0.71	0.361	4.47	141O-144N	1	1	1	1	1	7.654	11.292	7.605	-3.833	1.033	5.835
7nw2_A				USZ	LON-WEI-adc59df6-47				0.555	-0.497	-0.84	1.513	3.25	141O-144N	1	1	1	1	1	7.652	11.288	7.067																
7p35				AG7	Rupintrivir	P			1.133	-0.803	-0.328	-1.512	-7.983	141O-144N	1	1	1	1	1	7.672	11.571	6.325	0.775	-0.627	-1.242	-2.066	-4.604	141O-144N	1	1	1	1	1	7.675	11.708	6.403	-2.473	-8.763	5.296

PDB data are between 10/25/2020 of Tables 1&2 and 7/25/2021. The meaning of the table is the same as in Table S1 and S2.

Dataset S5. Summary of the ligand-free entries suppplemented to Dataset S2.

specirs	protein				comments	chain A													chain B											dimer		
						PC1					C-loop conformation								PC1					C-loop conformation									
	PDB ID	mutation	residues added to N-term	missing N-term residues		C-loop	E-loop	helical loop	linker	Domain III	main-chain HB within 138-144	HB 138-172[&]	HB 139-126[&]	HB 140-1[&]	HB 141-118[&]	HB 143-28[&]	distance 165Cα-140Cβ	distance 165Cα-141Cβ	distance 2-214	C-loop	E-loop	H-loop	Linker	Domain III	main-chain HB within 138-144	HB 138-172[&]	HB 139-126[&]	HB 140-1[&]	HB 141-118[&]	HB 143-28[&]	distance 165Cα-140Cβ	distance 165Cα-141Cβ	distance 2-214	PC1 Domain III	PC2 Domain III	distance between two 285 Cα's
SARS-CoV-2	7alh					0.636	-2.049	-1.375	-2.807	-5.759	141O-144N	1	1	1	1	1	7.680	11.709	6.348														-0.001	-8.365	5.311
	7ali					0.753	-2.213	-1.198	-2.865	-3.978	141O-144N	1	1	1	1	1	7.575	11.647	6.535	0.757	-2.5	-1.058	-2.602	-5.837	141O-144N	1	1	1	1	1	7.639	11.711	6.228	1.462	-8.126	5.371
	7ar5				Cys300 is mono-oxydized to be CSO (S-hydroxycysteine).	0.811	-2.061	-1.426	-3.421	-6.709	141O-144N	1	1	1	1	1	7.410	11.330	6.163															0.001	-11.236	5.128
	7ar6					1.087	-0.822	-1.824	0.063	-8.112	141O-144N	1	1	1	1	1	7.725	11.573	6.056														0.001	-11.978	5.224
	7avd_A				Chain B binds a ligand.	0.883	-2.801	-0.069	-2.74	-14.464	141O-144N	1	1	1	1	1	7.373	11.221	5.982															-6.19	-9.655	5.526
	7baj					0.942	-2.449	-1.349	-2.915	-4.169	141O-144N	1	1	1	1	1	7.803	11.780	6.357														0	-7.002	5.390
	7bb2					0.425	0.387	-0.678	1.463	4.169	141O-144N	1	1	1	1	1	7.709	11.547	7.300	0.569	0.165	0.549	2.133	-2.63	141O-144N	1	1	1	1	1	7.842	11.536	6.815	2.431	0.35	5.470
	7ca8_B			SG of A,B	Chain A is ligand-bound. C-terminal residues 299-306 do not exist.															-1.435	-0.101	14.532	1.823	3.105		1	0	0	0	1	8.494	12.241		1.22	12.886	8.610
	7cam		G	GSGF of A, GSG of B		0.059	-0.376	0.895	1.398	-7.559	141O-144N	0	0	0	1	1	8.856	10.881		-0.245	-0.991	0.698	1.895	1.817	141O-144N	0	0	0	1	1	8.278	12.439		-4.699	3.107	5.443
	7djr					0.938	-1.533	-1.517	-0.712	-5.647	141O-144N	1	1	1	1	1	7.386	11.325	6.250														0	-10.532	5.119
	7jpy				Cys300 is mono-oxydized to be CSO (S-hydroxycysteine).	0.7	-2.417	-0.97	-2.571	-5.07	141O-144N	1	1	1	1	1	7.618	11.688	6.263															0.001	-8.018	5.309
	7jst					0.478	0.279	-0.097	1.567	-7.276	141O-144N	1	1	1	1	1	7.566	11.629	6.373														0.001	-9.11	5.644
	7kph					1.023	-1.26	-1.82	-0.413	-5.845	141O-144N	1	1	1	1	1	7.773	11.685	6.482														0	-9.564	5.221
	7kvl_B		GAM	GAM of B																-10.682	0.978	2.764	2.033	13.676	139O-142N 140O-143N	0	0	0	0	0	9.745	13.864	8.234	-4.725	19.553	10.009
	7kvr_A		GAM	GAM of A, GAMS of B		-1.601	-0.683	0.247	1.716	6.974	140O-143N	1	0	0	0	1	11.843	11.777	8.794														-2.043	13.813	9.542
	7l13_B				Chain A is ligand-bound.															0.663	-0.788	1.062	0.677	-9.457	141O-144N	1	1	1	1	1	7.712	11.527	6.523	4.833	-1.553	5.504
	7lfe_B		GAM	GAMS of B	Chain A is ligand-bound.															-10.781	0.656	3.138	1.765	10.497	139O-142N 140O-143N	0	0	0	0	0	9.799	14.050	8.583	-2.15	17.03	9.750
	7lkd					0.892	-2.188	-0.967	-3.292	-4.491	141O-144N	1	1	1	1	1	7.177	11.307	6.567	0.969	-2.785	-0.625	-2.418	-4.213	141O-144N	1	1	1	1	1	7.299	11.253	6.231	0.155	-7.167	5.396
	7lke					1.074	-3.14	-0.738	-1.898	-5.129	141O-144N	1	1	1	0	1	7.453	11.530	6.356														-0.001	-7.963	5.243
	7m8m_B				Chain A is ligand-bound.															0.765	-0.114	1.017	-0.204	-7.913	141O-144N	1	1	1	1	1	7.779	11.348	6.764	4.404	-2.185	5.293
	7m8o_B				Chain A is ligand-bound.															0.704	-0.011	1.217	0.428	-7.398	141O-144N	0	1	1	1	1	7.997	11.491	6.997	4.64	-3.14	5.541
	7m8p_B				Chain A is ligand-bound.															0.703	-0.997	0.832	0.369	-5.201	141O-144N	1	1	1	1	1	7.753	11.618	6.774	1.054	-0.663	5.795
	7mbg					0.718	-0.176	0.466	1.756	0.964	141O-144N	1	1	1	1	1	7.697	11.435	6.699	0.682	-0.094	10.458	1.979	-3.146	141O-144N	0	1	1	1	1	7.660	11.530	6.646	-1.085	-2.909	5.468
	7mhf				100K	0.879	-1.205	-1.356	-0.812	-6.173	141O-144N	1	1	1	1	1	7.672	11.642	6.248														0.002	-10.255	5.086
	7mhg				240K	0.818	-1.878	-1.289	-1.365	-4.237	141O-144N	1	1	1	1	1	7.841	11.899	6.231														0.001	-8.918	5.276
	7mhh				277K	0.698	-1.816	-1.281	-2.841	-2.029	141O-144N	1	1	1	1	1	7.353	11.274	6.333														0	-5.477	5.760
	7mhi				298K	0.736	-1.974	-1.442	-2.767	-2.689	141O-144N	1	1	1	1	1	7.741	11.752	6.437														0	-5.184	5.849
	7mhj				298K	0.647	-2.213	-1.203	-2.713	-3.047	141O-144N	1	1	1	1	1	7.412	11.336	6.478														0.001	-5.647	5.772
	7mhk				310K	0.671	-1.889	-1.331	-2.135	-2.195	141O-144N	1	1	1	1	1	7.473	11.400	6.398														0	-5.064	5.817
	7n5z	C145S				0.747	-1.933	-1.436	-2.73	-4.753	141O-144N	1	1	1	1	1	7.753	11.452	6.439														-0.002	-6.214	5.228
	7nt1_A				Chain B binds a ligand.	0.854	0.182	0.757	1.399	-6.322	141O-144N	1	1	1	1	1	7.792	11.583	6.625															-5.269	1.449	5.668
	7nt2_A				Chain B binds a ligand.	0.546	-0.277	1.173	1.623	-6.073	141O-144N	1	1	1	1	1	7.942	12.021	6.580															-5.61	2.08	5.805
	7nt3_A				Chain B binds a ligand.	0.858	0.31	0.924	0.243	-6.297		1	1	1	1	1	7.807	11.648	6.897															-4.666	1.96	5.644
	7ntv_A				Chain B binds a ligand.	0.748	0.056	0.867	1.353	-5.26	141O-144N	1	1	1	1	1	7.862	11.879	6.444															-4.559	1.334	5.772
	7nuk_A				Chain B binds a ligand.	0.757	0.346	0.836	1.444	-4.113	141O-144N	1	1	1	1	1	7.841	11.517	6.695															-3.833	1.033	5.835
	7nw2_B				Chain B binds a ligand.															0.712	0.174	0.854	1.901	-3.742	141O-144N	1	1	1	1	1	7.686	11.324	6.962	2.171	-0.607	5.577

Dataset S6. Summary of ligand binding supplemented to Dataset S4.

species	PDBid	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker					Ligand interactions
		BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	
SARS-CoV	6w79	AB	1	1	0	1	0	0	1	1	1	11	11	1	11	1	1	11	0	0	0	1	1	1	0	0	0	CE
	7k0g	AB	0	0	0	1	1	1	11	1	1	1	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEHL
	7k0h	A	0	1	0	11	0	0	11	1	1	11	0	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
	7lcp	AB	0	0	0	1	1	0	11	1	1	0	1	21	11	11	1	11	0	0	1	0	0	11	0	0	0	CE
	7lcq	AB	0	0	0	1	0	0	11	0	1	1	0	21	11	11	1	11	0	0	1	0	1	11	0	0	0	CE
SARS-CoV-2	7a1u	AB	0	0	0	1	1	0	0	0	1	0	0	1	0	1	1	0	0	0	0	1	1	11	0	0	0	L
	7abu[x]	AB	0	0	0	0	0	0	0	1[#]	11[#]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7adw	AB	0	0	0	0	0	0	1	1	1	0	0	20	11	1	0	1	0	0	0	0	0	0	0	0	0	
	7aeg	AB	0	0	0	1	0	0	1	1	0	11	1	21	11	11	1	11	0	1	0	0	1	1	1	0	1	CEL
	7aeh	AB	1	1	0	11	0	0	1	1	1	11	11	21	11	11	1	1	0	0	0	0	0	0	0	0	0	CE
	7af0[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7aga[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7aha	AB	0	0	0	1	0	0	0	0	11	11	0	21	0	1	0	0	0	0	0	0	0	0	0	0	0	C
	7ak4	AB	0	0	0	0	1	0	0	0	0	0	0	0	0	0	21	11	0	1	0	1	1	1	10	0	11	EL
	7amj[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7ans	AB	0	0	0	1	1	0	0	0	1	1	0	11	0	1	1	0	0	0	0	1	1	1	0	0	0	
	7aol[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7ap6	AB	0	0	0	1	1	1	11	1	0	0	0	1	11	1	1	1	0	0	0	1	0	0	0	0	0	H
	7aph[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7aqe	AB	1	0	0	1	1	0	0	0	1	0	0	0	0	0	0	11	1	1	0	0	0	11	0	0	0	
	7aqi[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7aqj	AB	0	0	0	0	1	0	0	0	1	1	0	21	0	1	1	0	0	0	0	0	0	0	0	0	0	
	7arf[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7avd																											
	7awr[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7aws	AB	0	0	0	11	1	0	0	1	11	0	0	21	1	1	11	0	0	0	0	1	1	1	0	0	0	CH
	7awu	AB	0	0	1	1	0	0	0	0	0	1	1	11	1	1	0	0	0	0	0	0	0	0	0	0	0	
	7aww[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7ax6[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7axm[x]	AB	0	0	0	0	0	0	0	1[#]	1[#]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7axo[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7ay7	AB	1	0	0	1	1	0	1	1	1	0	1	21	1	0	0	1	0	0	0	0	0	0	0	0	0	C
	7b3e	A	1	0	0	1	1	0	0	0	0	1	0	21	0	1	1	10	0	0	0	1	1	1	0	0	0	
	7bak	AB	0	0	0	10	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7bal	AB	0	0	0	10	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7be7	A	0	0	0	1	0	0	0	0	1	1	1	21	1	11	1	11	0	1	0	0	0	11	1	1	1	EL
	7bfb[x]	A	0	0	0	0	1	0	0	0	0	1	0	21	0	0	0	0	0	0	0	1	0	1	0	0	0	
	7bgp	A	0	0	0	1	0	0	0	0	1	1	0	21	1	11	1	11	0	1	0	0	0	11	1	1	1	EL
	7ca8	A	0	0	0	1	0	0	0	0	0	0	0	1	0	1	1	0	0	0	0	1	1	1	1	0	1	L
	7cb7	A	0	0	0	1	1	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
	7cut	AB	0	0	0	1	1	0	1	0	1	11	1	21	1	1	1	11	0	0	0	1	1	1	0	0	0	C
	7cuu	A	0	0	0	1	1	0	1	0	1	1	0	21	1	11	1	11	0	1	0	1	0	11	1	1	1	EL
	7dk1	A	0	0	0	20	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7dpp	AB	1	1	1	1	0	0	0	0	0	1	0	21	0	1	1	0	0	0	0	1	0	0	0	0	0	R
	7dpu	A	1	1	1	1	1	1	0	0	0	1	0	21	0	0	1	11	0	0	0	1	1	1	0	0	0	RH
	7dpv	A	1	0	0	1	0	1	0	0	0	11	0	21	0	1	1	10	0	0	0	1	1	1	0	0	0	
	7dpv	B	1	0	0	1	1	1	0	0	0	11	0	21	0	1	1	10	0	0	0	1	1	1	0	0	0	H
	7e18	AB	1	0	1	1	1	0	11	1	1	0	1	21	11	11	1	11	0	1	1	0	1	11	1	1	0	CEL
	7e19	AB	1	0	0	1	1	0	11	1	1	1	1	21	11	11	1	11	0	0	1	0	0	1	1	1	1	CEL
	7ein	A	0	0	0	1	1	1	0	0	1	1	0	21	0	11	1	11	0	0	0	1	0	1	1	0	0	EH
	7fay	AB	0	0	0	1	1	0	1	1	1	11	0	21	11	1	1	11	0	0	0	0	0	1	0	0	0	CE
	7faz	A	0	0	0	1	1	1	1	1	1	11	11	21	11	1	1	11	0	0	0	1	1	1	0	0	0	CEH
	7jpz	AB	0	0	0	1	1	1	11	1	1	11	1	21	11	1	1	11	1	1	1	1	1	1	0	0	0	CEH
	7jq0	AB	0	0	0	1	1	0	11	0	1	1	1	21	11	11	1	11	0	1	1	1	0	1	1	1	0	CEL
	7jq1	AB	0	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	0	1	1	1	1	1	1	1	1	CEHL

species	PDBid	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker					Ligand interactions
		BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	
SARS-CoV	7k0h	B	0	1	0	11	0	0	11	1	1	11	0	11	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
SARS-CoV-2	7avd	B	0	0	0	1	11	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	1	0	0	0	H
	7b3e	B	1	1	1	1	0	0	0	0	0	1	0	21	0	1	1	10	0	0	0	1	1	0	0	0	0	R
	7be7	B	0	0	0	1	1	0	0	0	1	1	0	21	1	11	1	11	0	1	0	0	0	11	1	1	1	EL
	7bfb[x]	B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7bgp	B	0	0	0	1	0	0	0	0	1	1	0	21	1	11	1	11	0	0	0	0	0	11	1	1	1	EL
	7cb7	B	0	0	0	11	1	0	11	0	1	0	1	21	11	11	1	11	0	0	1	0	0	11	0	0	0	CEH
	7cuu	B	0	0	0	1	1	0	1	1	1	11	0	21	1	11	1	11	1	1	0	1	0	11	1	1	1	CEL
	7dk1	B	0	0	0	20	0	0	0	0	0	0	0	20	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7dpu	B	1	0	0	1	1	1	0	0	0	1	0	21	0	1	1	11	0	0	0	1	1	1	0	0	0	H
	7dpv	C	1	1	0	1	0	1	0	0	0	1	0	21	0	1	1	0	0	0	0	1	1	1	0	0	0	
	7dpv	D	1	1	0	1	0	1	0	0	0	1	0	21	0	1	1	10	0	0	0	1	1	1	0	0	0	
	7ein	B	0	0	0	1	1	1	0	0	0	1	0	21	0	11	1	11	0	0	0	1	0	1	1	0	0	EH
	7faz	B	0	0	0	1	1	1	1	1	1	11	11	21	11	1	1	11	0	0	0	1	1	0	0	0	0	CEH

7jq2	AB	0	0	0	1	1	1	11	1	1	11	0	21	11	10	1	11	0	1	1	1	1	1	1	1	1	CEHL																											
7jq3	AB	0	0	0	1	0	1	11	1	1	11	0	21	11	11	1	11	0	1	0	1	1	1	1	1	1	CEL																											
7jq4	AB	0	0	0	1	1	1	11	1	1	11	1	21	11	11	1	11	1	1	1	1	1	1	1	1	1	CEHL																											
7jq5	AB	0	0	0	1	1	1	11	1	1	11	0	21	11	11	1	11	0	1	1	1	1	1	1	1	0	CEHL																											
7jsu	AB	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL																											
7jt0	AB	0	0	0	1	0	0	0	0	0	0	0	21	0	1	1	0	0	0	0	0	0	0	0	0	0																												
7jt7	AB	0	0	0	1	0	0	11	1	1	11	0	21	11	11	1	11	1	1	1	1	0	11	1	1	1	CEL																											
7jw8	A	0	0	0	1	0	0	11	0	1	10	1	21	11	11	1	11	0	1	1	0	0	11	1	1	1	CEL	B	0	1	0	1	1	0	11	0	1	11	0	21	11	11	1	11	0	1	1	0	0	11	1	0	1	CEL
7jw8	C	1	1	1	1	0	0	11	1	1	1	0	21	11	11	1	11	0	1	1	0	0	11	1	0	1	RCEL	D	0	0	0	1	1	0	11	0	1	10	0	21	11	11	1	11	0	1	1	0	0	11	1	1	1	CEL
7k0e	A	0	0	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE	B	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
7k0f	A	0	1	0	11	0	0	11	1	1	11	0	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL	B	0	1	0	11	0	0	11	0	1	11	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
7kvl[x]	A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0																												
7kvr[x]																												B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
7kx5	AB	1	1	1	1	1	1	1	1	1	11	11	1	11	1	1	11	0	0	0	1	1	1	0	0	0	RCEH																											
7kyu	AB	0	0	0	1	0	0	0	0	0	0	0	21	0	1	1	0	0	0	0	1	1	0	0	0	0																												
7l0d	AB	1	1	1	1	1	0	1	1	1	11	1	1	11	1	0	1	0	0	0	1	1	1	0	0	0	RC																											
7l10	AB	1	1	0	1	1	0	1	1	1	1	0	1	11	1	1	11	0	0	0	0	1	0	0	0	0	CE																											
7l11	A	1	1	0	1	1	0	1	1	1	1	0	1	11	1	1	11	1	0	0	0	1	1	0	0	1	CE	B	1	1	0	1	1	0	1	1	1	1	11	1	11	1	1	11	1	0	0	0	1	1	1	0	0	CE
7l12	AB	1	11	0	1	1	0	1	1	1	11	0	11	11	1	1	11	0	1	0	0	1	1	1	0	0	RCE																											
7l13	A	1	10	0	1	1	0	1	1	1	11	0	11	11	0	1	11	0	1	0	0	0	1	1	0	0	RCE																											
7l14	A	1	1	0	1	1	0	1	1	1	1	0	1	11	1	1	11	1	0	0	0	1	1	1	0	1	CEL	B	1	1	0	0	1	0	1	1	1	1	1	1	11	1	1	11	0	1	0	0	1	1	1	0	1	CEL
7l5d	AB	1	0	0	11	1	0	1	1	1	0	0	10	11	11	1	1	0	0	0	0	0	0	0	0	0	EH																											
7lb7	AB	1	1	0	11	0	0	0	0	1	11	1	21	0	11	1	11	0	1	0	1	1	11	1	1	1	CEL																											
7lbn	AB	0	0	0	1	0	0	1	1	1	11	0	21	0	11	1	11	0	0	0	1	0	0	0	0	0	CE																											
7lco	AB	0	0	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	1	0	1	0	0	CE																											
7lcs	AB	0	0	0	1	1	1	11	1	1	1	0	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEHL																											
7lct	AB	0	0	0	1	1	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	1	1	1	1	0	CEL																											
7ldl	A	0	0	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEL	B	0	0	0	1	1	0	11	0	1	1	1	21	11	11	1	11	0	0	1	1	1	1	1	1	0	CEL
7ldx[x]	AB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0																												
7lfe	A	0	0	0	11	1	0	0	0	0	0	0	11	0	1	1	11	0	0	0	1	0	1	0	0	0	H																											
7lkr	A	0	0	0	11	0	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE	B	0	0	0	11	0	1	11	1	1	0	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEHL
7lks	A	0	0	0	1	0	0	11	1	1	11	0	21	11	11	1	11	1	1	1	1	0	11	0	0	0	CE	B	0	0	0	1	0	0	0	0	1	1	1	21	11	11	1	11	0	0	1	1	0	11	1	0	0	EL
7lkt	A	0	0	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEL	B	0	0	0	1	0	0	10	0	1	1	1	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL
7lku	A	0	0	0	11	0	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE	B	0	0	0	11	1	0	11	1	1	0	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEHL
7lkv	A	0	0	0	11	1	0	11	0	1	0	1	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CEH	B	0	0	0	11	0	0	11	0	1	0	1	21	11	11	1	11	1	1	1	1	0	11	0	0	0	CE
7lkw	A	0	0	0	10	0	0	11	1	1	0	0	21	11	11	1	11	1	1	1	1	1	11	0	0	0	CEL	B	0	0	0	11	1	0	11	0	1	0	1	21	11	11	1	11	0	1	1	1	0	11	0	0	0	CEH
7lkx	A	0	0	0	11	0	0	11	0	1	0	0	21	11	11	1	11	1	1	1	1	0	11	0	0	0	CE	B	0	0	0	11	1	0	1	0	1	0	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	EH
7lmc	A	0	0	0	0	1	0	1	1	1	1	1	1	11	1	1	11	1	1	0	0	1	11	0	1	1	CEL	B	0	0	0	1	1	0	1	1	1	11	0	1	11	11	1	11	0	1	1	0	1	11	11	0	1	CEL
7lmc	C	0	0	0	1	1	0	1	1	1	1	0	1	11	1	1	11	1	1	1	1	1	1	0	1	10	CEL	D	0	0	0	1	1	0	1	1	1	11	1	11	11	11	1	11	1	1	0	1	0	11	1	1	0	CEL
7ltj	AB	0	0	0	1	1	0	1	1	1	11	1	1	11	0	0	11	0	0	1	0	0	1	0	0	0	CE																											
7lyh	AB	0	0	0	1	1	0	11	1	1	0	0	11	11	11	1	11	0	1	1	1	1	1	1	0	0	CEL																											
7lyi	AB	0	0	0	1	1	0	11	0	1	1	1	21	11	11	1	11	0	0	1	1	1	0	0	0	0	CE																											
7lzt	AB	0	0	0	11	0	0	11	1	1	0	0	21	11	11	1	11	0	1	1	1	1	11	0	0	0	CEL																											
7lzu	A	0	0	0	11	1	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEHL	B	0	0	0	1	1	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	1	11	1	0	0	CEL
7lzv	A	0	0	0	11	0	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL	B	0	0	0	11	0	1	11	1	1	0	0	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEHL
7lzw	A	0	0	0	10	0	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEL	B	0	0	0	11	0	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
7lzx	A	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	1	1	1	0	11	0	0	0	CE	B	0	0	0	1	0	0	11	0	1	1	1	21	11	11	1	11	1	1	1	1	0	11	0	0	0	CE
7lzy	AB	0	0	0	11	1	0	1	0	1	0	0	21	11	11	1	11	0	1	1	1	0	11	1	0	0	EHL																											
7lzz	AB	0	0	0	11	0	1	11	0	1	0	0	21	11	11	1	11	0	1	1	1	0	11	0	0	0	CEH																											
7m00	A	0	0	0	11	0	1	1	0	1	0	0	21	11	11	1	11	1	1	1	1	1	11	1	0	0	EHL	B	0	0	0	11	0	1	1	0	1	0	0	21	11	11	1	11	1	1	1	1	1	11	1	0	0	EHL
7m01	A	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEL	B	0	0	0	11	1	0	11	0	1	0	1	21	11	11	1	11	0	0	1	1	1	11	1	0	0	CEHL
7m02	A	0	0	0	1	0	0	11	1	1	1	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEL	B	0	0	0	1	0	0	11	0	1	1	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL
7m03	A	0	0	0	11	0	0	11	1	1	0	0	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEL	B	0	0	0	1	0	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL
7m04	A	0	0	0	11	0	0	11	0	1	0	0	21	11	11	1	11	0	0	1	1	0	11	1	1	0	CEL	B	0	0	0	11	0	0	11	1	1	0	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL
7m8m	A	1	11	0	1	1	0	1	1	1	11	0	11	11	1	1	11	1	0	0	0	1	0	0	0	1	RCE																											
7m8n	A	1	11	0	1	1	0	1	1	1	11	0	11	11	0	1	11	1	1	0	0	0	1	1	0	1	RCE	B	1	11	0	1	0	0	1	1	1	11	0	11	11	0	1	11	1	1	0	0	1	1	1	0	1	RCEL
7m8o	A	1	11	0	1	0	0	1	1	1	11	0	11	11	1	1	11	0	1	0	0	0	1	1	0	0	RCE																											
7m8p	A	1	11	0	1	0	0	1	1	1	11	10	11	11	1	1	11	0	1	0	0	0	1	1	0	0	RCE																											
7m8x	AB	1	1	0	1	1	0	1	1	1	1	1	1	11	1	1	11	1	0	0	0	1	1	1	0	1	CEL																											
7m8y	AB	1	0	0	0	1	0	1	1	1	11	0	11	0	0	1	11	0	1	0	0	1	1	1	0	0	C																											

PDBid	BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	Ligand interactions
	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker					
7m8z	AB	1	0	0	0	0	0	1	1	11	11	0	11	11	1	1	11	1	1	0	0	1	1	1	0	1	CEL
7m90	AB	1	0	0	1	1	0	1	1	1	11	0	11	11	1	1	11	1	1	0	0	0	1	1	1	11	CEL
7m91	AB	1	0	0	1	0	0	1	1	11	11	0	11	11	0	1	11	0	0	0	0	0	1	0	0	1	CE
7mbi	A	0	0	0	1	0	0	11	0	1	11	0	21	11	11	1	11	0	0	0	1	1	11	1	1	0	CEL
7mbi	B	0	0	0	1	0	0	11	0	1	11	1	21	11	11	1	11	0	1	1	1	1	11	1	1	0	CEL
7mgr	AB	1	11	0	1	1	0	11	1	11	11	1	11	11	11	1	11	1	1	1	0	1	1	11	0	1	RCEL
7mgs	AB	1	11	0	1	1	0	11	1	11	11	0	11	11	11	1	11	0	1	1	0	1	1	11	0	1	RCEL
7mng	AB	1	1	0	11	1	0	0	0	1	11	0	21	0	1	1	1	0	0	0	0	0	1	0	0	0	CH
7mpb	A	0	0	0	0	0	0	1	1	11	1	1	11	10	0	0	1	0	0	0	0	0	0	0	0	0	C
7mrr	AB	0	0	0	1	1	0	0	1	1	0	0	21	1	11	1	11	0	0	0	0	0	1	1	0	0	E
7n44	AB	1	11	0	1	1	0	1	1	1	11	0	11	11	1	1	11	1	1	0	0	1	1	1	1	1	RCEL
7n6n	A	0	0	0	1	0	0	1	1	1	1	1	11	11	11	1	11	0	1	1	1	1	1	11	1	0	CEL
7n89	A	1	11	0	1	1	0	11	1	1	11	1	11	11	11	1	11	0	1	1	0	1	11	11	1	1	RCEL
7n8c	AB	0	0	0	1	1	0	1	0	1	11	1	21	11	0	0	11	0	0	1	0	0	1	0	0	0	CE
7nbr	AB	0	0	0	11	1	1	0	0	1	11	0	21	0	11	1	11	1	1	0	1	0	1	1	0	1	CEHL
7nbs	AB	1	1	0	11	1	0	0	0	1	11	0	21	0	11	1	11	1	1	0	0	1	11	1	1	1	CEHL
7nby[x]	A	0	0	0	1	1	1	0	0	0	0	0	21	0	1	1	0	0	0	0	1	11	11	0	0	0	HL
7nf5	AB	0	0	0	1	1	0	1	0	1	1	0	21	1	11	1	11	0	1	0	1	0	11	1	1	1	EL
7ng3	A	0	0	0	1	1	0	1	0	0	1	0	21	1	11	1	11	1	1	0	1	0	11	1	1	1	EL
7ng6	A	0	0	0	1	0	0	1	0	0	1	0	21	0	11	1	11	1	0	0	1	1	11	1	1	1	EL
7nt1																											
7nt2																											
7nt3																											
7ntv																											
7nuk																											
7nw2	A	0	0	0	1	1	0	1	1	1	10	11	21	11	1	1	11	0	0	0	1	1	1	0	0	1	CEL
7p35	A	1	1	0	1	1	0	11	1	1	11	1	21	11	0	1	11	0	1	1	1	1	1	11	1	0	CEL

PDBid	BC	T25	T26	L27	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	Ligand interactions
	MC	interface			H-loop			C-loop				interface		I&II		E-loop					I&II	Linker					
7m8z																											
7m90																											
7m91																											
7mbi	D	0	0	0	1	0	0	11	0	1	11	0	21	11	11	1	11	0	0	1	1	1	1	1	1	0	CEL
7mbi	C	0	0	0	1	0	0	11	1	0	1	0	21	11	11	1	11	0	0	1	1	1	11	1	1	0	CEL
7mgr																											
7mgs																											
7mng																											
7mpb	B	0	0	0	0	0	0	1	1	1	1	0	1	11	0	0	1	0	0	1	0	0	0	0	0	0	C
7mrr																											
7n44																											
7n6n	B	0	0	0	1	1	0	1	1	1	1	1	1	1	0	1	11	0	1	1	1	1	1	0	1	0	CEL
7n89	B	1	11	0	1	1	0	1	1	1	11	0	11	11	11	1	11	0	1	0	1	1	11	11	0	1	RCEL
7n8c																											
7nbr																											
7nbs																											
7nby[x]	B	0	0	0	1	0	1	0	0	0	0	0	21	0	11	1	0	0	0	0	1	1	0	0	0	0	
7nf5																											
7ng3	B	0	0	0	1	0	0	1	0	1	1	0	21	1	11	1	11	1	1	0	1	0	11	1	1	1	EL
7ng6	B	0	0	0	1	0	0	1	0	1	1	0	21	1	11	1	10	0	1	0	1	0	11	1	1	1	EL
7nt1	B	0	0	0	1	1	0	1	0	1	1	1	21	11	0	1	1	0	0	0	0	0	1	0	0	0	C
7nt2	B	0	0	0	1	1	0	0	0	1	1	0	21	0	1	1	11	0	0	0	1	1	1	0	0	0	
7nt3	B	0	0	0	1	1	1	1	1	1	0	0	0	11	1	1	11	0	0	0	1	1	1	0	0	0	EH
7ntv	B	1	1	0	1	1	0	0	0	1	1	0	21	0	0	0	0	0	0	0	0	0	0	0	0	0	
7nuk	B	0	1	0	1	0	0	0	0	0	11	0	21	0	0	0	0	0	0	0	0	0	0	0	0	0	
7nw2																											
7p35	B	0	1	1	1	1	0	11	1	0	11	1	21	11	10	1	11	0	1	1	1	1	1	1	1	0	CEL

PDB data are between 10/25/2020 of Tables 1&2 and 7/25/2021. The meaning of the table is the same as in Table S4. The minor 14 binding sites other than the extraordinary binding sites (Table shown below) are Lys5(1), Gly15(1), Thr24(6), Asn28(1), Pro39(3), Cys44(13), Thr45(3), Ser46(6), Ala70(1), Lys97(1), Gly146(1), Ser147(1), Gln256(1), Ser301(2), where the numbers of the parentheses are the number of contacts.

[#]the inter-protomer contact.

The ligand binding at sites outside the major binding sites (the entry name with x).

7abu	A:401		B:141,142 A: 252,253,256,297	7axm	A:502		B:118,141,142 A:213,252,253,256,296,297,300,301	7nby	A:401		A: 41,44,49,54,187,188,189
7af0	A:504		A:273,274	7axo	A:506		A:237,271,272,273,274,275,276,285,287		A:402		A: 1,2,3,210,213,214,300
7aga	A:401		A:107,108,109,110,153,202,203,249,292,293,294,298	7bfb	A:401		A:44,45,49,187,189		A:403		A: 41,145,164,165,189
7amj	A:409		B:142 A:213,253,256,297,300,301		A:402		A:143,145		A:406		A: 100,101,102,156
7aol:	A:403		A:103,104,105,176,178		A403		A:100,101,102,156		B:406		B: 44,53,54,57,188
7aph	A:401		A:252,253,255,256,297,300,301		B:1002		B:100,102,156		B:401		B: 1,2,141,213,214,300
7aqi	A:401		A:252,253,256,297,300		B:1001		B:256,297,300,301		B:402		B: 39,41,145,164,165,187
7arf	A:401		A:100,101,155,156	7kvl	A:503		A:233,237,269,273		B:403		B: 101,156
7awr	A:401		A:33,99,100,101,102	7kvr	A:703		A:83,84				
7aww	A:401		A:33,34,94,95,98	7ldx	A:509		A:132,133,196,198,235,239,240,241				
7ax6	A:401		A:100,101,102,156		B:402		B:132,133,196,198,235,239,240,241				

Residue number without underline is for nonpolar contact, with single underline for polar contact, and with double underline for covalent bond.

Supporting data S7 Summary of entries of MERS-CoV 3CL protease

ligand	protein				ligand				comments	Chain A									Chain B								
										C-loop conformation									C-loop conformation								
	PDB ID	mutation	residues added to N-term	missing N-terminal residues	name in PDB	name by authors	peptide or peptide mimic[$]	Ki, IC_{50}*, EC_{50}+ (μM)		main-chain HB within 141-147 (138-145)[#]	HB 141-175 (138-172)[#]	HB 142-129 (139-126)[#]	HB 143-1 (140-1)[#]	HB 144-121 (141-118)[#]	HB 146-28 (143-28)[#]	distance 168Cα-143Cβ (165-140)[#]	distance 168Cα-144Cβ (165-141)[#]	HB 2-217 (2-214)[#]	main-chain HB within 141-147 (138-145)[#]	HB 141-175 (138-172)[#]	HB 142-129 (139-126)[#]	HB 143-1 (140-1)[#]	HB 144-121 (141-118)[#]	HB 146-28 (143-28)[#]	distance 168Cα-143Cβ (165-140)[#]	distance 168Cα-144Cβ (165-141)[#]	HB 2-217 (2-214)[#]	distance between two 285 Cα's
ligand bound	4rsp				PRD_002174	6	p	3.6	C145 is CSO and does not bind the ligand	144O-147N	1	0	1	1	1	7.414	10.957	1									6.123
	4wme_AB	C148A				C-term of another molecule	p		chain BD are ligand-free. A(C) bind C-term of C(A)	144O-147N	1	0	1	1	1	7.485	10.867	1	144O-147N	1	0	1	1	1	7.556	10.982	1	6.153
	4wmf_A	C148A				C-term of another molecule	p		chain BC are ligand free A binds C-term of C	144O-147N	1	0	1	1	1	7.294	10.603	1									5.956
	4ylu_AB				R30	11		>100*		144O-147N	1	0	1	1	1	7.5	11.073	1	144O-147N	1	0	1	1	1	7.549	11.173	1	7.174
	4ylu_CD				R30	11		>100*		144O-147N	1	0	1	1	1	7.589	11.175	1	144O-147N	1	0	1	1	1	7.475	10.935	1	6.132
	5wkj		MH6	MH5	K36,B1S	GC376	p		K36 and,B1S are stereoisomers, and not distinguished	144O-147N	1	0	0[&]	1	1	7.225	10.955	0									6.762
	5wkk		MH6	MH4	B3G,AW4	GC813	p		B3G and AW4 are stereoisomers, and not distinguished	144O-147N	1	0	0[&]	1	1	7.278	10.744	0									6.603
	5wkl		MH6	MH4	B3J, AVY	10c	p	0.7*	B3J and AVY are stereoisomers, and not distinguished	144O-147N	1	0	0[&]	1	1	7.332	10.946	0									7.26
	5wkm		MH6	MH4	B6Y, N02	10e		7.5*	B6Y and N02 are stereoisomers, and not distinguished	144O-147N	1	0	0[&]	1	1	7.3	11.024	0									7.636
	6vgy		MH6	MH4 of A,B	QZJ	6b		0.33*		144O-147N	0[$]	0	0[&]	1	1	7.298	11.006	0	144O-147N	0[$]	0	0[&]	1	1	7.356	11.099	0	9.495
	6vgz		MH6	MH4 of A,B	QZG	6d		0.41*		144O-147N	0[$]	0	0[&]	1	1	7.3	11.061	0	144O-147N	0[$]	0	0[&]	1	1	7.348	11.181	0	9.624
	6vh0		MH6	MH4 of A,B	QZD	6g		0.12*		144O-147N	0[$]	0	0[&]	1	1	7.193	10.862	0	144O-147N	0[$]	0	0[&]	1	1	7.352	11.144	0	9.289
	6vh1		MH6	MH4 of A,B	QZ7	6h		0.07*		144O-147N	0[$]	0	0[&]	1	1	7.284	11.074	0	144O-147N	0[$]	0	0[&]	1	1	7.287	11.067	0	9.842
	6vh2		MH6	MH4 of A,B	QZ4	7i		1.9*		144O-147N	0[$]	0	0[&]	1	1	7.317	11.066	0	144O-147N	0[$]	0	0[&]	1	1	7.434	11.123	0	9.758
	6vh3		MH6	MH4 of A, MH6 of B	QYS	7j	p	0.1*		144O-147N	0[$]	0	0[&]	1	1	7.486	11.369	0	144O-147N	0[$]	0	0	1	1	7.32	11.132	0	10.103
ligand free	4wmd_AB	C148A								144O-147N	1	0	1	1	1	7.238	10.959	0	144O-147N	1	0	1	1	1	7.277	10.989	1	6.293
	4wmd_C	C148A								144O-147N	1	0	1	1	1	7.215	10.962	1									6.116
	4wme_CD	C148A							chain AD are ligand bound	144O-147N	1	0	1	1	1	7.426	10.866	1	144O-147N	1	0	1	1	1	7.4	10.817	1	6.191
	4wmf_B	C148A							chain A is ligand bound										144O-147N	1	0	1	1	1	7.215	10.755	1	5.956
	4wmf_C	C148A		1-10 of C					chain C is monomeric. Its core is maintained, but domain III rotates about 180 deg.	144O-147N	0	0	0	1	1	8.071	11.316	0									
	5c3n									144O-147N	0	0	1	1	1	7.87	11.145	0	144O-147N	0	0	1	1	1	7.571	11.064	1	6.581

The residue numbers in parenthesis is the corresponding number for SARS-CoV-2 $3CL^{pro}$.
$ HB 141-175 is replaced by HB 140-175.
& HB 143-1 is replaced by HB 142-2.

Table S8 Ligand binding at protein residues of MERS-CoV 3CL protease.

		interface	H-loop			C-loop						E-loop							Linker						Ligand interactions
entry	chain	M25	H41	L49	Y54	F143	L144	C145	G146	S147	C148	H166	Q167	M168	E169	L170	A171	H175	D190	K191	Q192	V193	H194	Q195	
4rsp	A	0	1	0	0	11	1	1	10	1	21	11	11	1	11	0	0	1	1	10	11	11	1	11	CEL
4wme_AB	A	0	11	0	0	11	1	1	11	1	11	11	11	1	11	1	0	1	1	1	11	11	1	1	CEL
4wme_CD	D	0	11	0	0	11	1	0	11	0	11	11	11	1	11	1	0	1	1	1	1	1	1	0	CEL
4wmf_AB	A	0	11	0	0	11	1	1	11	1	11	11	11	1	11	1	1	1	1	1	11	1	11	0	CEL
4ylu_AB	A	1	1	1	1	1	1	1	0	0	11	11	0	1	11	0	0	0	1	1	1	0	0	0	EH
4ylu_AB	B	1	1	1	0	1	1	1	0	0	1	11	0	1	11	0	0	0	1	1	1	0	0	0	E
4ylu_CD	C	1	1	1	0	1	1	1	0	0	1	11	0	1	11	0	0	0	1	1	1	0	0	0	EH
4ylu_CD	D	1	1	1	1	1	1	1	0	0	11	11	0	1	11	0	0	0	1	1	1	0	0	0	EH
5wkj	A	0	11	1	0	11	1	1	0	0	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
5wkk	A	0	1	1	0	11	1	1	1	1	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEL
5wkl	A	0	11	1	1	11	1	1	0	1	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CEH
5wkm	A	0	0	0	0	11	0	1	1	1	21	11	11	1	11	0	0	1	1	1	0	0	0	0	CE
6vgy	A	0	1	1	0	1	1	1	1	1	21	11	11	1	11	0	1	1	1	0	11	0	0	0	CE
	B	0	0	1	0	11	0	0	1	1	21	11	11	1	11	1	1	1	1	1	11	0	0	0	CEL
6vgz	A	0	1	0	0	11	0	1	1	0	21	11	11	1	11	0	1	1	1	1	11	0	0	0	CEL
	B	0	0	0	0	11	0	0	1	0	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL
6vh0	A	0	1	0	0	11	1	1	1	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL
	B	0	0	1	0	11	0	0	1	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CEL
6vh1	A	0	1	1	0	11	0	0	1	1	21	11	11	1	11	0	0	1	0	0	11	0	0	0	CE
	B	0	0	1	0	11	0	0	1	1	21	11	11	1	11	0	0	1	1	0	11	0	0	0	CE
6vh2	A	0	1	1	1	11	1	1	1	1	21	11	10	1	11	0	0	1	1	1	11	1	0	11	CELH
	B	0	1	1	1	11	0	1	1	1	21	11	11	1	11	0	0	1	1	1	11	0	0	0	CELH
6vh3	A	0	1	0	0	11	0	0	1	1	21	11	11	1	11	1	1	1	1	1	11	1	0	11	CEL
	B	0	1	0	0	11	0	0	1	0	21	11	11	1	11	0	1	1	1	0	11	1	1	0	CEL
MERS-CoV		M25	H41	L49	Y54	F143	L144	C145	G146	S147	C148	H166	Q167	M168	E169	L170	A171	H175	D190	K191	Q192	V193	H194	Q195	
ratio of occurrence		0.17	0.79	0.58	0.21	1.00	0.58	0.67	0.75	0.63	1.00	1.00	0.83	1.00	1.00	0.21	0.29	0.83	0.96	0.71	0.96	0.33	0.25	0.17	
SARS-CoV-2		T25	H41	M49	Y54	F140	L141	N142	G143	S144	C145	H163	H164	M165	E166	L167	P168	H172	D187	R188	Q189	T190	A191	Q192	
ratio of occurrence		0.25	0.94	0.66	0.18	0.72	0.65	0.80	0.83	0.49	0.99	0.74	0.88	0.89	0.90	0.22	0.47	0.56	0.68	0.54	0.80	0.56	0.38	0.43	

The contacts occurring in only one chain, L27, C44, S46 and A193, are not listed in the table.