Supplemental Material

Molecular Basis of the Potential Interaction of SARS-Cov-2 Spike Protein to CD147 in COVID-19 Associated Lymphopenia.

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Table S1: Atoms and residues constituting pockets 1 and 6 on the surface of CD147 as proposed by the CASTp server and used, subsequently, for the docking prediction.

Pocket ID	Residue	Atoms
1	Ser78	O
1	Asp79	CA, C, O, CB, CG, OD1
1	Gln81	N, CA, C, O, CB
1	Trp82	CB, CG, CD1, CD2, CE2, CE3, NE1, CZ2, CZ3, CH2
1	Gly103	CA, C
1	Pro104	N, C, O, CB, CG, CD
1	Pro105	C, O, CD
1	Arg106	CA, CG, CD
1	Ser193	C, O
1	Asp194	CB, CG, OD1, OD2
6	Arg106	C, O, CB, CZ, NH1, NH2
6	Val107	CA, C
6	Lys108	N, O, CB, CG, CD, CE
6	Lys127	C, O, CB, CG, CD
6	Ser128	N, CA, C
6	Glu129	N, OE2

Table S2: Binding residues of CD147 as predicted by the CPROT server.

Predicted (interacting) residues	Surrounding Residues
54, 56, 57, 58, 59, 60, 61, 62, 74, 82, 83, 102, 106, 129, 130, 131, 132, 133, 135, 164, 165, 188, 190, 191, 192,	37, 38, 63, 64, 65, 73, 75, 77, 78, 79, 80, 81, 84, 86, 92, 100, 103, 104, 105, 107, 108, 127, 128, 136, 137, 138, 162, 163, 166, 186, 189, 193, 194,

Table S3: Interacting residues in both proteins, spike-RBD and CD147, as detected by the PDBePISA server.

ASA	Accessible Surface Area, Å²	BSA	Buried Surface Area, Å²	Δ^iG	Solvation energy effect, kcal/mol	|||	Buried area percentage, one bar per 10%

HSDC: Residues making **H**ydrogen/**D**isulphide bond, **S**alt bridge or **C**ovalent bonds.

##	Spike-RBD	HSDC	ASA	BSA	Δ^iG
1	A:ARG 403		71.98	40.03 |||||	- 0.69
2	A:LYS 417		80.24	26.44 ||||	0.42
3	A:GLY 446		50.11	6.99 ||	- 0.08
4	A:TYR 449		133.37	60.01 |||||	0.31
5	A:TYR 453		31.07	25.75 ||||||||	- 0.22
6	A:LEU 455		36.30	29.62 ||||||||	0.47
7	A:PHE 456		63.72	5.63 |	0.09
8	A:PRO 479		98.14	8.20 |	0.13
9	A:CYS 480		14.67	0.74 |	-0.01
10	A:ASN 481		145.19	85.22 |||||	-0.48
11	A:GLY 482		59.90	0.62 |	0.01
12	A:VAL 483		97.77	85.12 ||||||||	1.36
13	A:GLU 484	HS	102.42	80.85 |||||||	-0.46
14	A:GLY 485		41.95	38.00 |||||||||	0.53
15	A:PHE 486		182.11	30.97 ||	0.26
16	A:CYS 488		8.73	0.37 |	-0.00
17	A:TYR 489		98.92	43.33 |||||	0.69
18	A:PHE 490		83.47	1.51 |	0.02
19	A:LEU 492		19.35	0.49 |	-0.01
20	A:GLN 493		75.48	69.66 |||||||||	-0.75
21	A:SER 494		35.32	27.69 |||||||	0.05
22	A:TYR 495		15.20	14.91 ||||||||	0.24
23	A:GLY 496	H	37.98	37.98 ||||||||	0.19
24	A:PHE 497		1.72	1.72 |||||||||	0.03
25	A:GLN 498		66.09	47.00 |||||||	-0.59
26	A:PRO 499		53.98	2.33 |	-0.03
27	A:THR 500		121.79	86.06 |||||||	0.39
28	A:ASN 501	H	37.85	37.85 ||||||||	-0.31
29	A:GLY 502	H	42.83	32.72 |||||||	0.30
30	A:VAL 503		111.37	56.17 |||||	0.79

31	A:TYR 505	H	108.34	102.39 |||||||||	0.58
32	A:GLN 506		25.08	10.92 |||||	-0.12
##	CD147	HSDC	ASA	BSA	Δ^iG
1	B:THR 25		81.54	12.56 ||	0.20
2	B:VAL 26		24.53	8.35 ||||	-0.10
3	B:PHE 27		110.71	25.09 |||	0.40
4	B:THR 28		69.43	58.07 ||||||||	-0.25
5	B:THR 29		64.30	2.18 |	0.03
6	B:VAL 30		65.42	15.92 |||	0.23
7	B:GLU 84		69.78	19.34 |||	-0.19
8	B:ASN 98		90.23	17.27 ||	-0.03
9	B:ILE 99		10.56	10.56 |||||||||	0.17
10	B:GLN 100	H	70.76	37.62 |||||	0.05
11	B:LEU 101		34.64	14.40 |||||	0.23
12	B:HIS 102	S	83.35	63.36 |||||||	0.50
13	B:VAL 131		103.96	24.45 |||	0.39
14	B:PRO 132		23.21	10.37 |||||	0.17
15	B:PRO 133		63.94	38.85 ||||||	0.58
16	B:THR 135		99.50	96.06 |||||||||	0.61
17	B:ASP 136	H	89.18	89.18 ||||||||	-0.21
18	B:TRP 137	H	34.80	32.93 ||||||||	-0.29
19	B:ALA 138		24.27	22.43 ||||||||	0.36
20	B:TYR 140		57.06	32.65 |||||	-0.02
21	B:ALA 149		50.21	15.72 ||||	0.25
22	B:MET 151		116.82	69.85 |||||	2.09
23	B:ASN 152		97.54	33.23 ||||	0.08
24	B:VAL 160		37.73	16.58 |||||	0.27
25	B:SER 162		61.70	22.34 ||||	0.21
26	B:SER 163	H	64.92	12.92 ||	0.18
27	B:GLN 164		156.91	58.90 ||||	-0.34
28	B:ASN 186		21.11	12.29 |||||	-0.09
29	B:THR 188		49.01	49.01 ||||||||	0.54
30	B:SER 189		17.16	16.50 |||||||||	-0.17
31	B:SER 190		86.97	61.38 |||||||	0.57
32	B:LYS 191	HS	99.74	16.07 ||	-0.36
33	B:GLY 192		28.97	8.28 |||	0.03
34	B:SER 193		70.32	16.24 |||	-0.13

Table S4: Parameters of the interface of the interaction between the mutant spike and mutant CD147 as predicted by the PDBePISA server and the Hawkdock MM/GBSA calculations.

Spike		CD147		Interface		
Interface Residues	[a]Interface Surface,Å^2	Interface Residues	Interface Surface, Å^2	[b]Interface Surface, Å^2	[c]ΔG P-Value	MM/GBSA kcal/mol
25	10,205	28	10,042	925	0.398	– 60.64

Figure S1: Radius of gyration of the spike RBD-CD147 complex during the 100 ns Molecular Dynamics (MD) simulation.

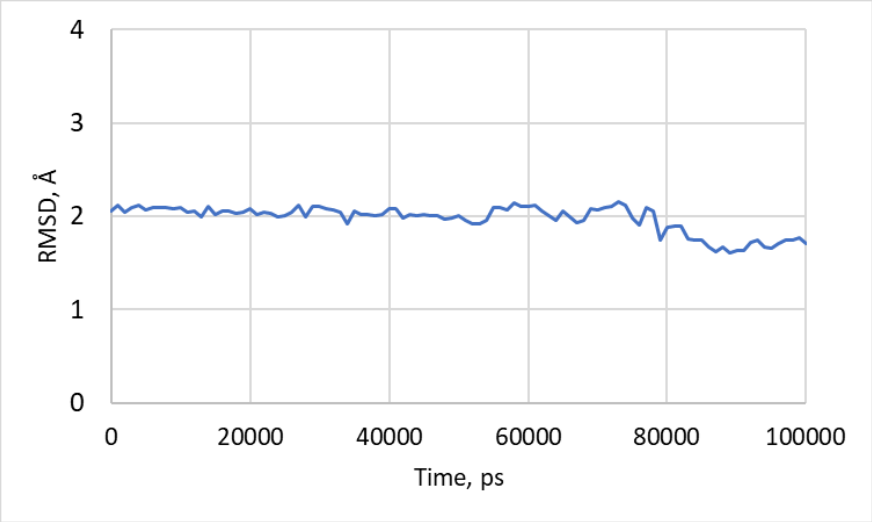

Figure S2: Proposed binding mode between the RBD of the 2003 SARS-CoV spike and CD147 as predicted by the HADDOCK server v2.2.

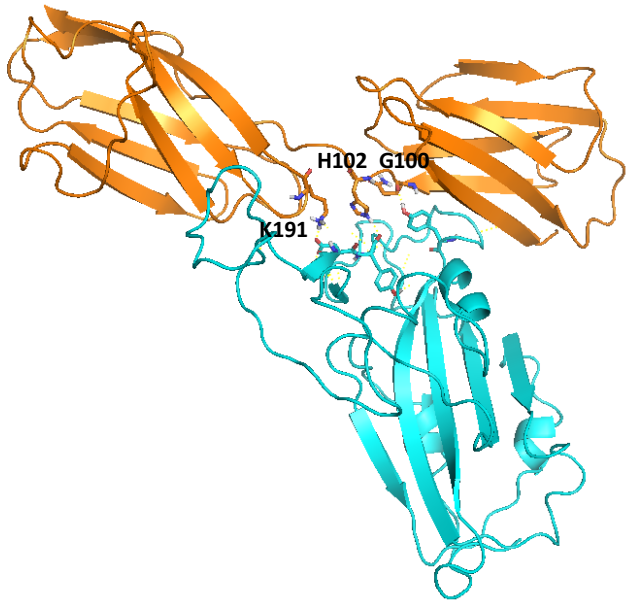

Figure S3: Polar interactions at the interface of the mutated proteins as predicted by the HADDOCK server v2.2. Key interacting residues are shown as sticks, while the proteins backbone is depicted as a transparent cartoon.

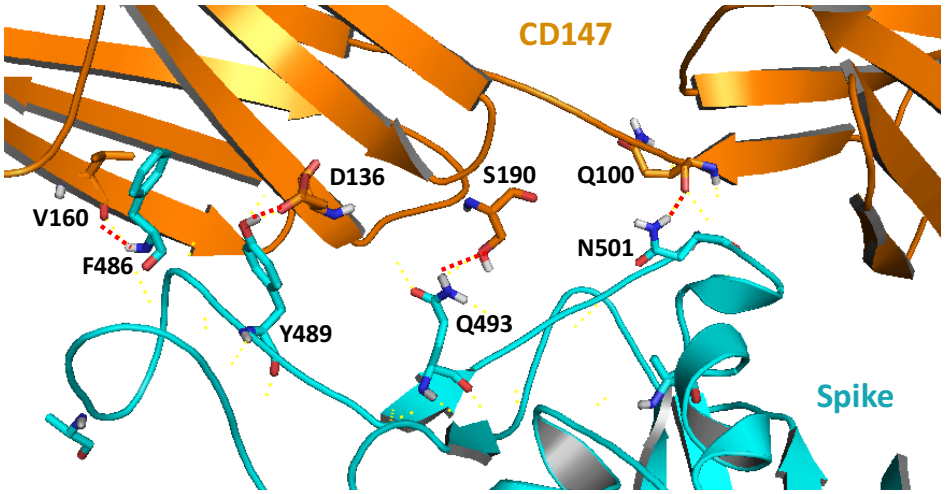

Figure S4: Backbone RMSD fluctuation of the mutated spike and CD147 proteins: the whole complex (blue), spike residues at the interface (orange), and CD147 residues at the interface (red) during the MD simulation.

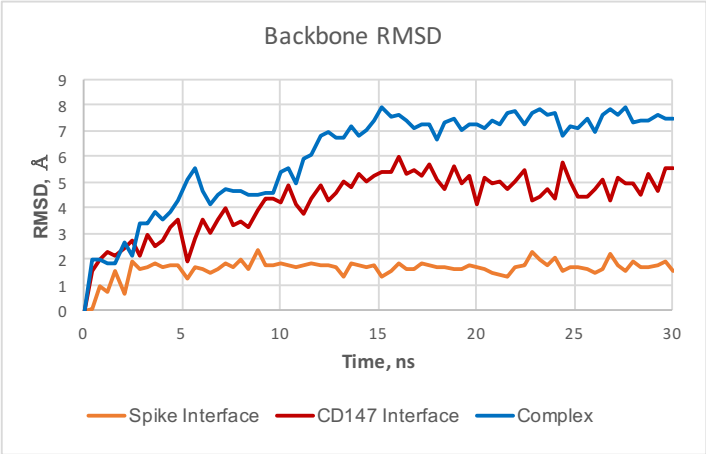

Figure S5: Residue contribution to the binding energy of the spike RBD-CD147 complex. Values are calculated as KJ/mol.