

**Supplementary material to:**

**Original article:**

**ANALYZING THE INTERACTION OF HUMAN ACE2 AND RBD  
OF SPIKE PROTEIN OF SARS-COV-2 IN PERSPECTIVE  
OFOMICRON VARIANT**

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**Supplementary Table 1: Details of the SARS-CoV-2 variants.** The first submitted complete genome sequences were retrieved from GISAID

SI No	Variants	Virus name	Accession ID	Submission Date	First detected in	Genome size (nucleotide)
<b>Reference</b>						
1	<b>(Wuhan Variant)</b>	WIV04	EPI_ISL_402124	11.01.2020	Wuhan	29891
<b>Variants of Concerns (VOCs)</b>						
2	B.1.1.7 GR/501Y.V1 (Alpha)	hCoV-19/England/CAMC-A58BA4/2020	EPI_ISL_596982	2020-10-27	United Kingdom	29763
3	B.1.351 GH/501Y.V2 (Beta)	hCoV-19/South Africa/KRISP-K004599/2020	EPI_ISL_660629	2020-11-27	South Africa	29848
4	B.1.1.28.1, alias P.1 GR/501Y.V3 (Gamma)	hCoV-19/Brazil/AM-FIOCRUZ-20143138FN-R2/2020	EPI_ISL_811149	2021-01-13	Brazil	29593
5	B.1.617 G/452R.V3 (Delta)	hCoV-19/India/MH-NEERI-NGP-29787/2021	EPI_ISL_1360328	2021-03-25	India	29839
6	B.1.1.529 (Omicron)	hCoV19/Botswana/R40B60_BHP_3321001247/2021	EPI_ISL_6640917	2021-11-23	Botswana / Hong Kong / South Africa	29684
<b>Variants of Interest (VOIs)</b>						
7	C.37, GR/452Q.V1 (Lambda)	hCoV-19/Peru/LIM-INS-436/2021	EPI_ISL_1111334	2021-03-01	Peru	29901
8	B.1.621, GH (Mu)	hCoV-19/Colombia/RIS-VG-3857/2021	EPI_ISL_3369952	2021-08-12	Colombia	29902
<b>Variants Under Monitoring (VUMs)</b>						
9	C.1.2	hCoV-19/South Africa/KRISP-K020275/2021	EPI_ISL_3447714	2021-08-17	South Africa	29803
10	B.1.617.1 (Kappa)	hCoV-19/India/WB-1931300244219/2021	EPI_ISL_1357699	2021-03-25	India	29781
11	B.1.630	hCoV-19/Dominican Republic/33884/2021	EPI_ISL_3045385	2021-07-22	Dominican Republic	29799
12	B.1.640	hCoV-19/Congo/FCRM-100-A32.28.09.21/2021	EPI_ISL_5592661	2021-10-27	Republic of Congo	29683
<b>Formerly Under Monitoring</b>						
13	B.1.427 B.1.429 (Epsilon)	hCoV-19/USA/CA-CZB-12872/2020	EPI_ISL_648527	2020-11-21	United States of America	29816
14	R.1	hCoV-19/Japan/IC-0386/2020	EPI_ISL_736897	2020-12-26	Asia / Japan	29770
15	B.1.466.2	hCoV-19/Indonesia/JI-ITDua-33281NT/2020	EPI_ISL_877419	2021-01-27	Indonesia	29890
16	B.1.1.318	hCoV-19/England/ALDP-115DB1E/2021	EPI_ISL_937654	2021-02-05	Europe / United Kingdom / England	29753
17	B.1.1.519	hCoV-19/Japan/IC-0377/2020	EPI_ISL_721617	2020-12-21	Asia / Japan	29768
18	C.36.3	hCoV-19/USA/TX-HMH-MCoV-27355/2021	EPI_ISL_1237137	2021-03-13	North America / USA / Texas / Houston	29804
19	B.1.214.2	hCoV-19/England/ALDP-CB0759/2020	EPI_ISL_760951	2021-01-04	Europe / United Kingdom / England	29750

**Supplementary Table 1 (cont.): Details of the SARS-CoV-2 variants.** The first submitted complete genome sequences were retrieved from GISAID

SI No	Variants	Virus name	Accession ID	Submission Date	First detected in	Genome size (nucleotide)
20	B.1.1.523	hCoV-19/Switzerland/GE-33615516/2021	EPI_ISL_1448584	2021-04-02	Europe / Switzerland / Geneva	29856
21	B.1.619	hCoV-19/Germany/BE-RKI-I-020766/2021	EPI_ISL_1150929	2021-03-04	Europe / Germany / Berlin	29809
22	B.1.620	hCoV-19/Lithuania/LTU000_NMVRI55624/2021	EPI_ISL_1579527	2021-04-13	Europe / Lithuania / Vilnius apskritis	29840
23	B.1.526 (Lota)	hCoV-19/USA/NY-Wadsworth-290357-01/2020	EPI_ISL_765494	2021-01-04	United States of America	29782
24	B.1.525 (Eta)	hCoV-19/England/CAMC-C769B3/2020	EPI_ISL_760883	2021-01-04	United Kingdom	29709
25	AV.1	hCoV-19/England/QEUI-148F257/2021	EPI_ISL_1595332	2021-04-15	United Kingdom	29764
26	AT.1	hCoV-19/Russia/PSK-16/2021	EPI_ISL_1259283	2021-03-16	Russian Federation	29803

**Supplementary Table 2: SWISS Model parameters of the predicted 3D structures of RBDs of SARS-CoV-2 variants**

Variants	Accession ID	Tem-plate Swiss model ID	Features of template used in generating S Protein model					Quality assess-ment of the S Protein model	
			Se-quence Identity	Method	Resolu-tion	Se-quence similar-ity	Cover-age	QMEAN	GMQE
B.1.1.7 GR/501Y.V1 (Alpha)	EPI_ISL_596982	7lww.1.A	100.00%	EM	-	0.63	1.00	0.78	0.84
B.1.351 GH/501Y.V2 (Beta)	EPI_ISL_660629	7lww.1.A	100.00%	EM	-	0.63	1.00	0.77	0.84
B.1.1.28.1, alias P.1 GR/501Y.V3 (Gamma)	EPI_ISL_811149	7v78.1.A	100.00%	EM	-	0.63	1.00	0.74	0.81
B.1.617 G/452R.V3 (Delta)	EPI_ISL_1360328	7cn4.1.A	89.69%	EM	-	0.59	1.00	0.70	0.77
B.1.1.529 (Omicron)	EPI_ISL_6640917	7lyq.1.A	94.17%	EM	-	0.61	1.00	0.74	0.81
C.37, GR/452Q.V1 (Lambda)	EPI_ISL_1111334	6zgf.1.A	89.69%	EM	-	0.59	1.00	0.72	0.78
B.1.621, GH (Mu)	EPI_ISL_3369952	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.427 B.1.429 (Epsilon)	EPI_ISL_648527	7cn4.1.A	89.69%	EM	-	0.59	1.00	0.70	0.77
R.1	EPI_ISL_736897	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.466.2	EPI_ISL_877419	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.1.318	EPI_ISL_937654	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.1.519	EPI_ISL_721617	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
C.36.3	EPI_ISL_1237137	7lww.1.A	100.00%	EM	-	0.63	1.00	0.78	0.84
B.1.214.2	EPI_ISL_760951	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.1.523	EPI_ISL_1448584	6xc4.1.A	99.10%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.619	EPI_ISL_1150929	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.620	EPI_ISL_1579527	6xc4.1.A	99.10%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
C.1.2	EPI_ISL_3447714	7lww.1.A	99.10%	EM	-	0.63	1.00	0.77	0.84
B.1.617.1 (Kappa)	EPI_ISL_1357699	7cn4.1.A	89.69%	EM	-	0.59	1.00	0.70	0.77
B.1.526 (Lota)	EPI_ISL_765494	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.525 (Eta)	EPI_ISL_760883	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80
B.1.630	EPI_ISL_3045385	7sbl.1.A	99.10%	EM	3.44 Å	0.63	1.00	0.73	0.10
B.1.640	EPI_ISL_5592661	7lww.1.A	98.21%	EM	-	0.63	1.00	0.78	0.84
AV.1	EPI_ISL_1595332	6xc4.1.A	99.10%	X-ray	2.34 Å	0.63	1.00	0.81	0.80
AT.1	EPI_ISL_1259283	6xc4.1.A	99.55%	X-ray	2.34 Å	0.63	1.00	0.80	0.80

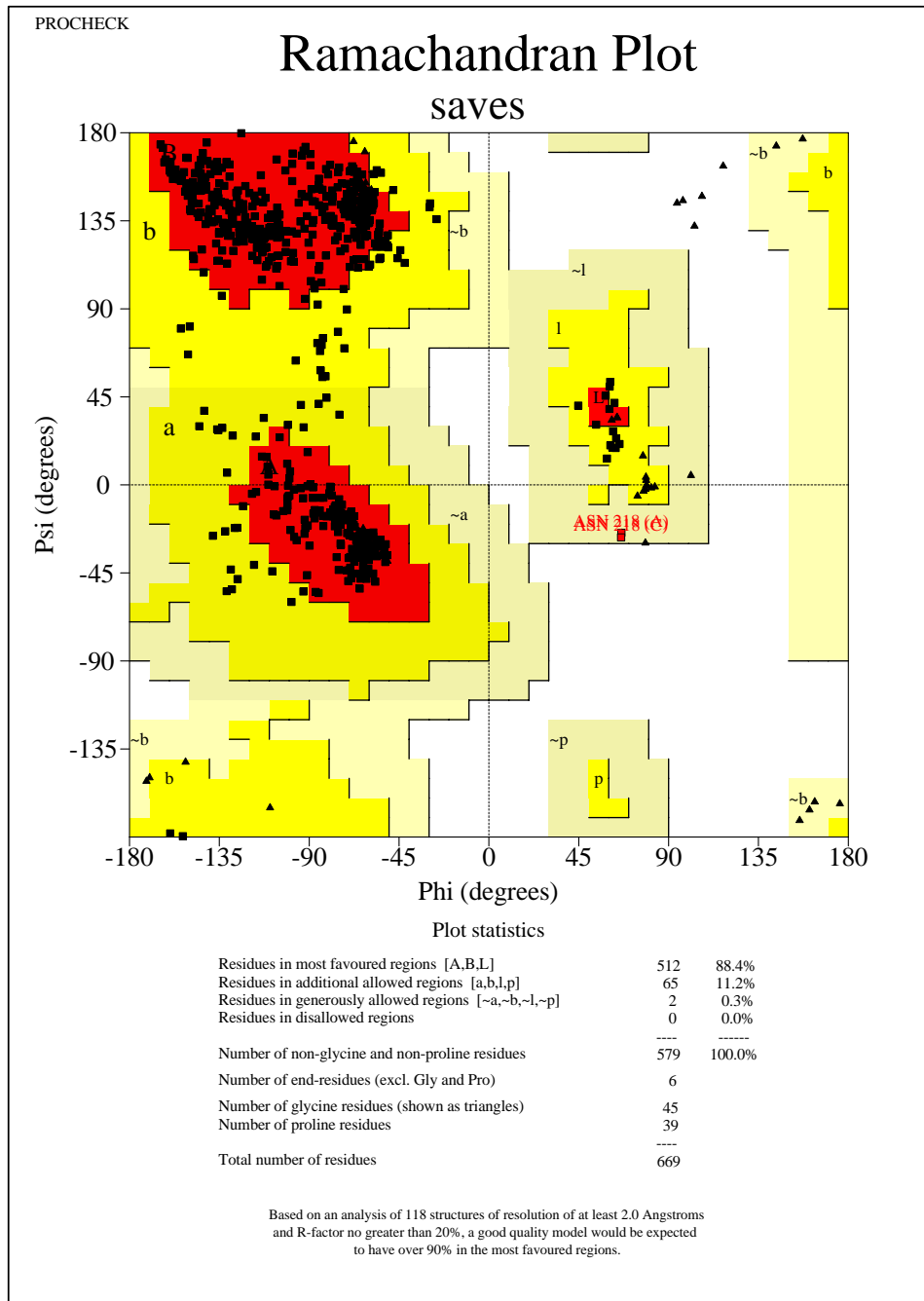


**Supplementary Table 3: S protein RBD model validation parameters obtained in SAVES and ProSA**

Variants	Accession ID	ERRAT	% of the residues have averaged 3D-1D score $\geq 0.2$	Ramachandran plot			G-factors	Z-Score
				core	allow	gener		
B.1.1.7 GR/501Y.V1 (Alpha)	EPI_ISL_596982	<b>94.5364</b>	93.12%	88.4%	11.2%	0.3%	-0.19	<b>-5.93</b>
B.1.351 GH/501Y.V2 (Beta)	EPI_ISL_660629	<b>94.0594</b>	91.18%	89.3%	10.5%	0.2%	-0.20	<b>-5.62</b>
B.1.1.28.1, alias P.1 GR/501Y.V3 (Gamma)	EPI_ISL_811149	<b>81.1287</b>	87.89%	87.0%	12.4%	0.3%	-0.14	<b>-5.48</b>
B.1.617 G/452R.V3 (Delta)	EPI_ISL_1360328	<b>93.6594</b>	93.72%	78.6%	21.2%	0.2%	-0.21	<b>-5.58</b>
B.1.1.529 (Omicron)	EPI_ISL_6640917	<b>96.6443</b>	95.37%	87.7%	11.8%	0.5%	-0.24	<b>-5.56</b>
C.37, GR/452Q.V1 (Lambda)	EPI_ISL_1111334	<b>80</b>	96.71%	83.2%	16.2%	0.5%	-0.22	<b>-5.52</b>
B.1.621, GH (Mu)	EPI_ISL_3369952	<b>97.076</b>	100.00%	90.6%	9.4%	0.0	-0.14	<b>-5.96</b>
B.1.427 B.1.429 (Epsilon)	EPI_ISL_648527	<b>93.8739</b>	93.57%	78.4%	20.9%	0.7%	-0.22	<b>-5.6</b>
R.1	EPI_ISL_736897	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.88</b>
B.1.466.2	EPI_ISL_877419	<b>96.5116</b>	96.98%	90.6%	9.4%	0.0%	-0.14	<b>-5.87</b>
B.1.1.318	EPI_ISL_937654	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.88</b>
B.1.1.519	EPI_ISL_721617	<b>97.0588</b>	97.99%	90.6%	9.4%	0.0%	-0.15	<b>-6.01</b>
C.36.3	EPI_ISL_1237137	<b>94.5364</b>	93.12%	88.4%	11.2%	0.3%	-0.19	<b>-5.93</b>
B.1.214.2	EPI_ISL_760951	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.14	<b>-5.99</b>
B.1.1.523	EPI_ISL_1448584	<b>96.5116</b>	98.49%	90.6%	9.4%	0.0%	-0.14	<b>-5.84</b>
B.1.619	EPI_ISL_1150929	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.88</b>
B.1.620	EPI_ISL_1579527	<b>97.076</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.92</b>
C.1.2	EPI_ISL_3447714	<b>94.4816</b>	93.12%	88.4%	11.2%	0.3%	-0.18	<b>-6</b>
B.1.617.1 (Kappa)	EPI_ISL_1357699	<b>93.6594</b>	93.72%	78.6%	21.2%	0.2%	-0.21	<b>-5.58</b>
B.1.526 (Lota)	EPI_ISL_765494	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.88</b>
B.1.525 (Eta)	EPI_ISL_760883	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.88</b>
B.1.630	EPI_ISL_3045385	<b>89.2857</b>	93.27%	86.5%	13.1%	0.3%	-0.25	<b>-5.28</b>
B.1.640	EPI_ISL_5592661	<b>94.01</b>	92.97%	88.3%	11.4%	0.3%	-0.19	<b>-6.08</b>
AV.1	EPI_ISL_1595332	<b>96.5116</b>	96.98%	90.6%	9.4%	0.0%	-0.13	<b>-5.87</b>
AT.1	EPI_ISL_1259283	<b>96.5116</b>	97.99%	90.6%	9.4%	0.0%	-0.13	<b>-5.88</b>

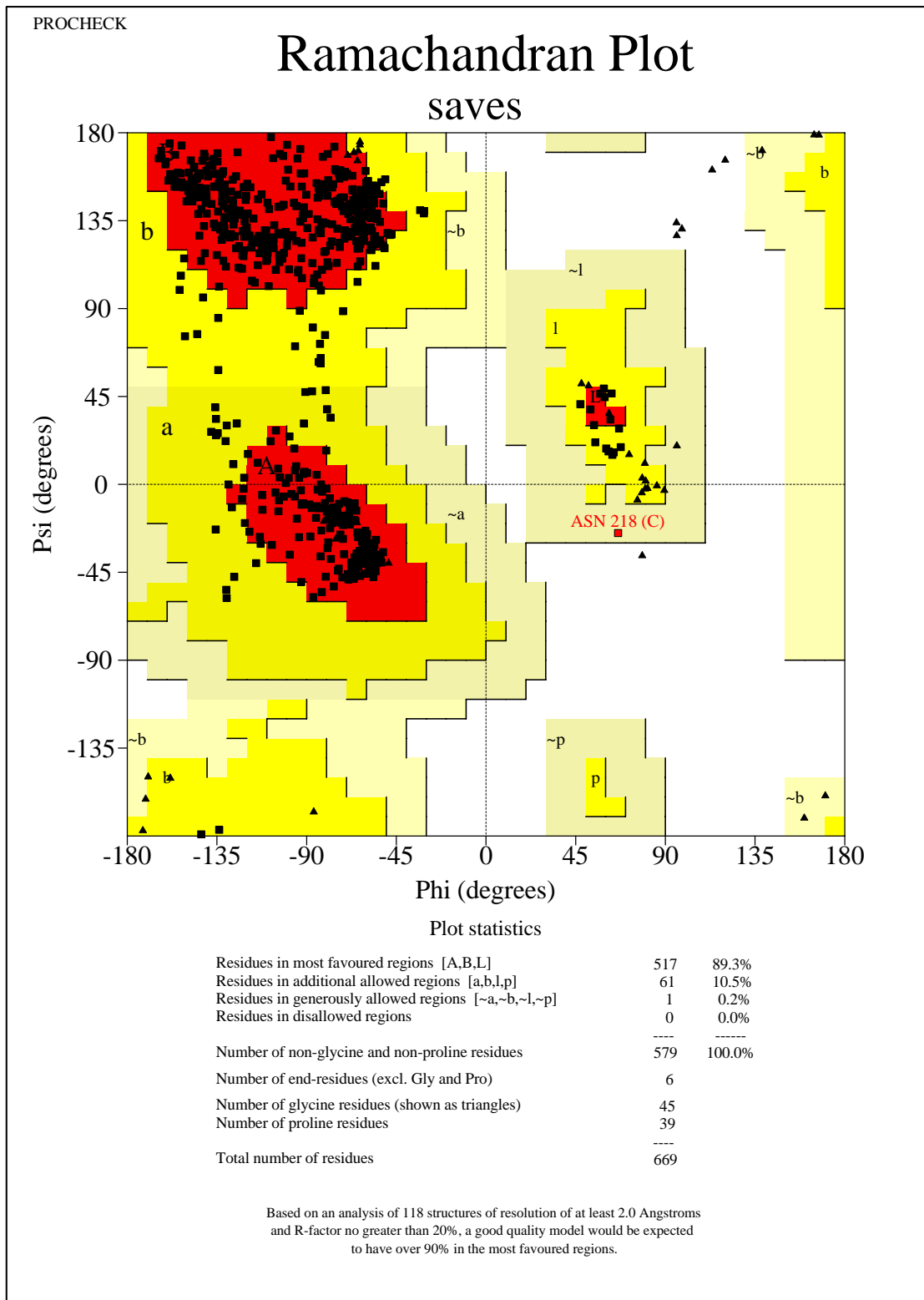
**Supplementary Table 4: Comparative analysis of interacting amino acid residues between hACE and Omicron RBD with all other variant RBD**

Variants	S Protein RBD			hACE2 Receptor		
	No. of Total Interacting Amino Acid(s)	No. of Amino Acid residues identical to Omicron	% of identical residues with Omicron	No. of Total Interacting Amino Acid(s)	No. of Amino Acid residues identical to Omicron	% of identical residues with Omicron
EPI ISL 402124(WIV04)	17	0	<b>0</b>	20	3	15
EPI ISL 596982(B.1.1.7 )	29	26	89.66	47	22	46.81
EPI ISL 660629(B.1.351 )	32	28	<b>90.32</b>	56	33	58.93
EPI ISL 811149(B.1.1.28.1)	25	13	52	34	1	2.94
EPI ISL 1360328(B.1.617)	33	27	81.82	58	25	43.10
EPI ISL 1111334(C.37)	21	21	<b>100</b>	46	14	30.43
EPI ISL 3369952(B.1.621)	33	0	<b>0</b>	32	5	15.63
EPI ISL 648527(B.1.427)	33	27	81.82	58	24	41.38
EPI ISL 736897(R.1)	23	0	<b>0</b>	34	2	5.88
EPI ISL 877419(B.1.466.2)	36	0	<b>0</b>	32	5	15.63
EPI ISL 937654(B.1.1.318)	32	0	<b>0</b>	34	2	5.88
EPI ISL 721617(B.1.1.519)	32	0	<b>0</b>	33	5	15.15
EPI ISL 1237137(C.36.3)	31	26	83.87	47	22	46.81
EPI ISL 760951(B.1.214.2)	33	0	<b>0</b>	30	5	16.67
EPI ISL 1448584 (B.1.1.523)	31	0	<b>0</b>	35	2	5.71
EPI ISL 1150929(B.1.619)	34	0	<b>0</b>	34	2	5.88
EPI ISL 1579527(B.1.620)	23	0	<b>0</b>	27	0	<b>0</b>
EPI ISL 3447714(C.1.2)	28	26	<b>92.86</b>	45	23	51.11
EPI ISL 1357699(B.1.617.1)	33	27	81.82	58	25	43.10
EPI ISL 765494(B.1.526)	32	0	<b>0</b>	34	2	5.88
EPI ISL 760883(B.1.525)	32	0	<b>0</b>	34	2	5.88
EPI ISL 3045385(B.1.630)	23	19	82.61	49	11	22.45
EPI ISL 5592661(B.1.640)	29	26	89.66	47	22	46.81
EPI ISL 1595332(AV.1)	34	0	<b>0</b>	33	2	6.06
EPI ISL 1259283(AT.1)	32	0	<b>0</b>	34	2	5.89

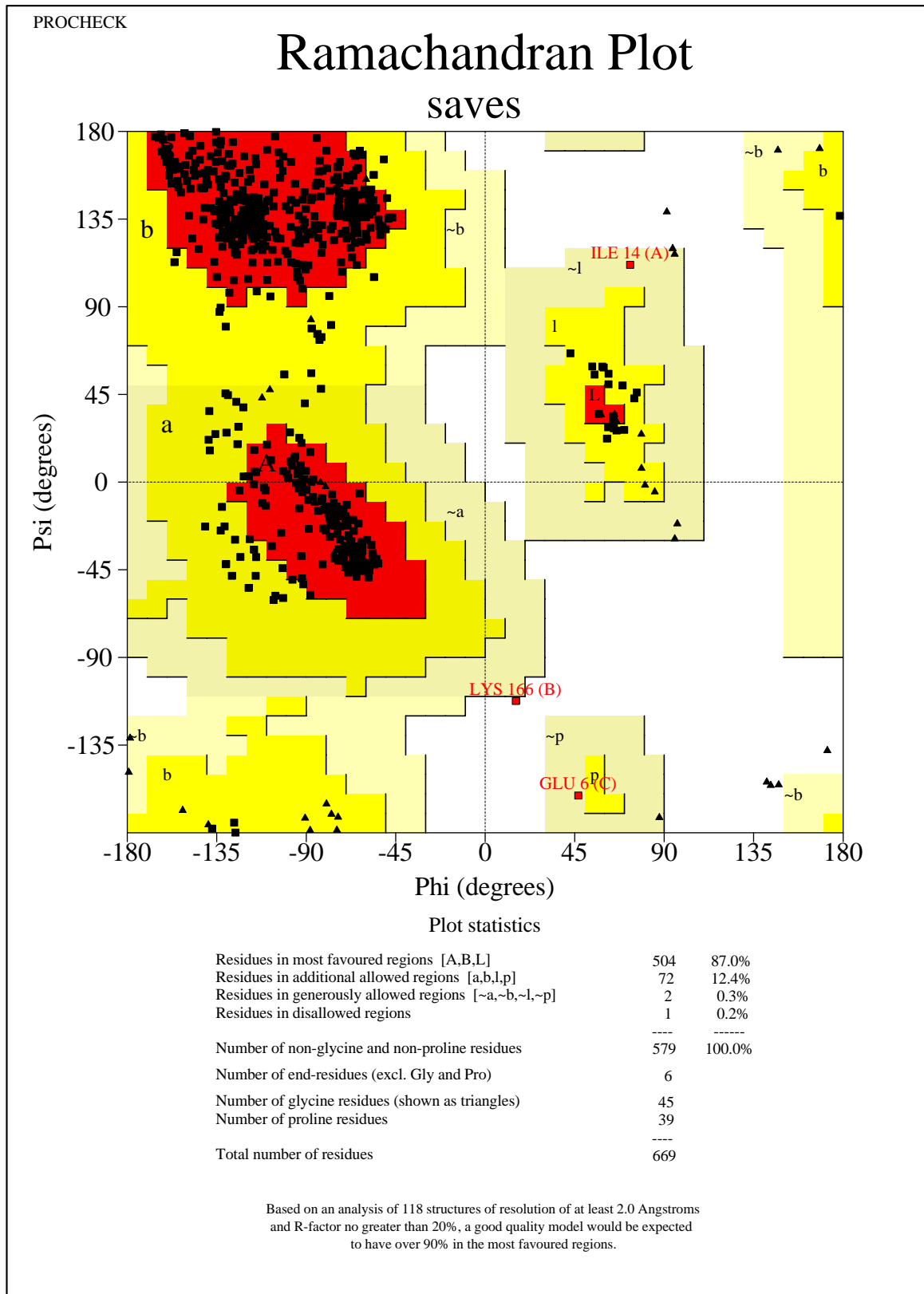


saves\_01.ps

**Supplementary Figure1(A):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.1.7(Alpha) variant (EPI\_ISL\_596982)

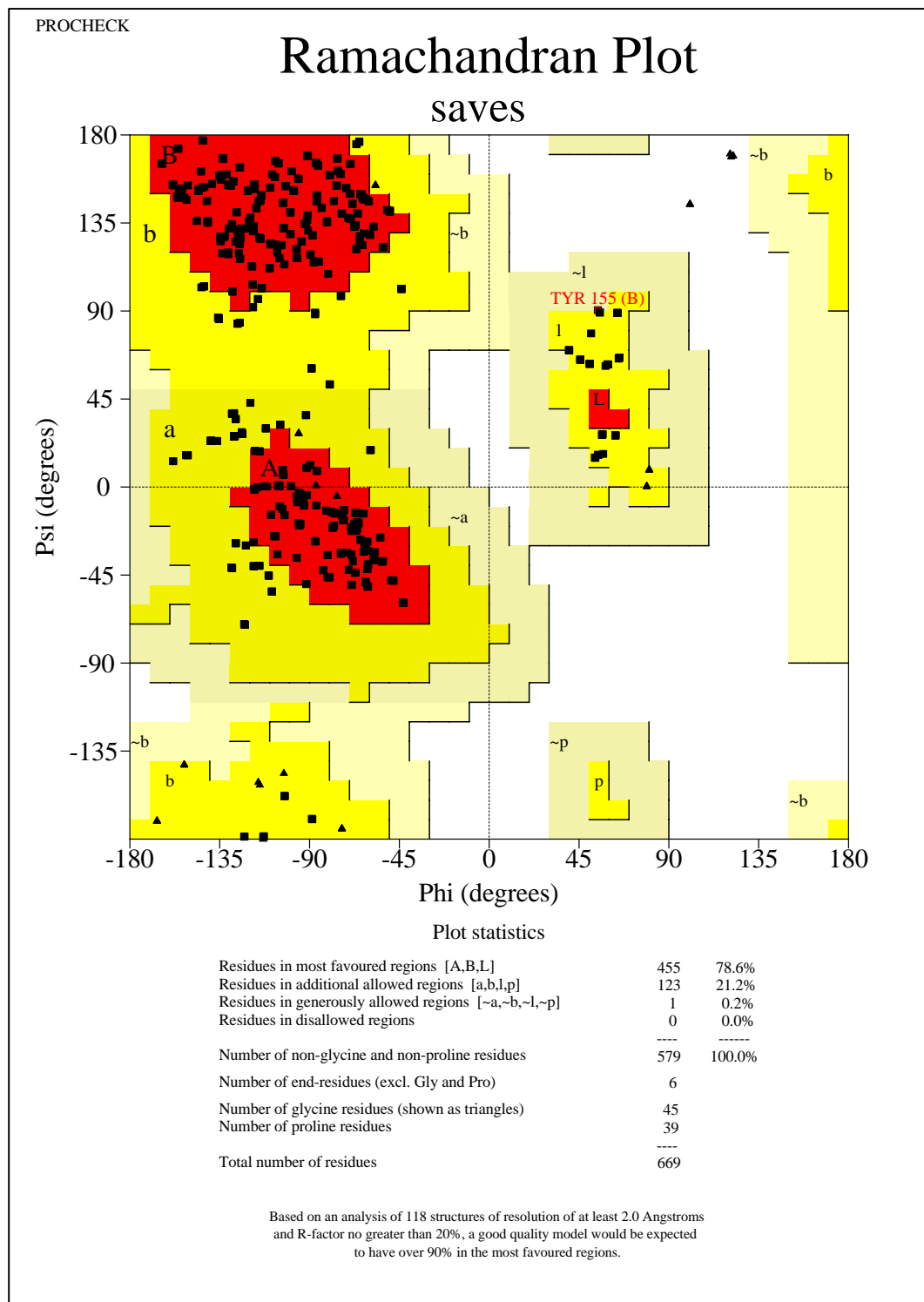


**Supplementary Figure 1(B):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.351 (Beta) variant (EPI\_ISL\_660629)

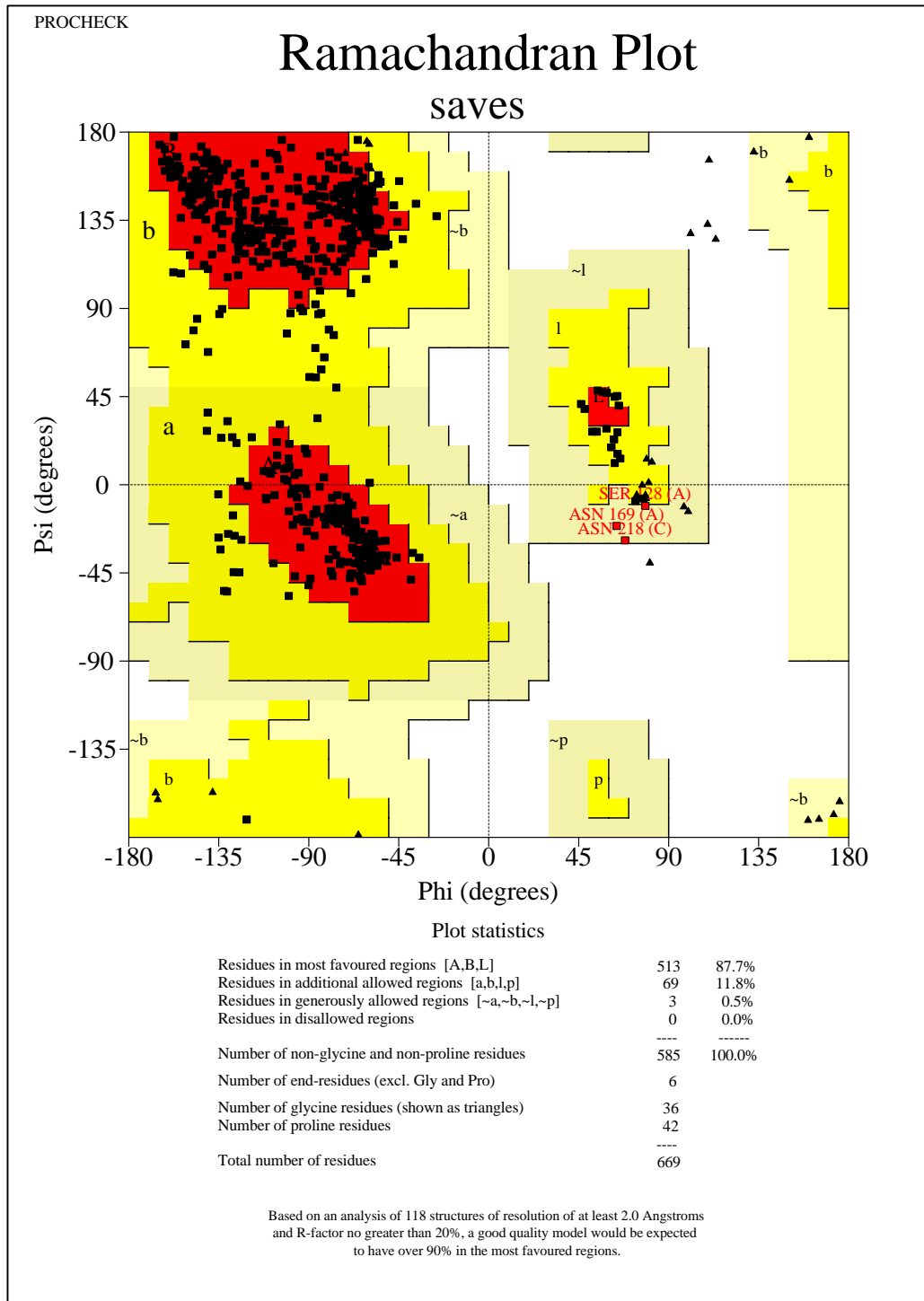


saves\_01.ps

**Supplementary Figure 1(C):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.1.28.1(Gamma) variant EPI\_ISL\_811149

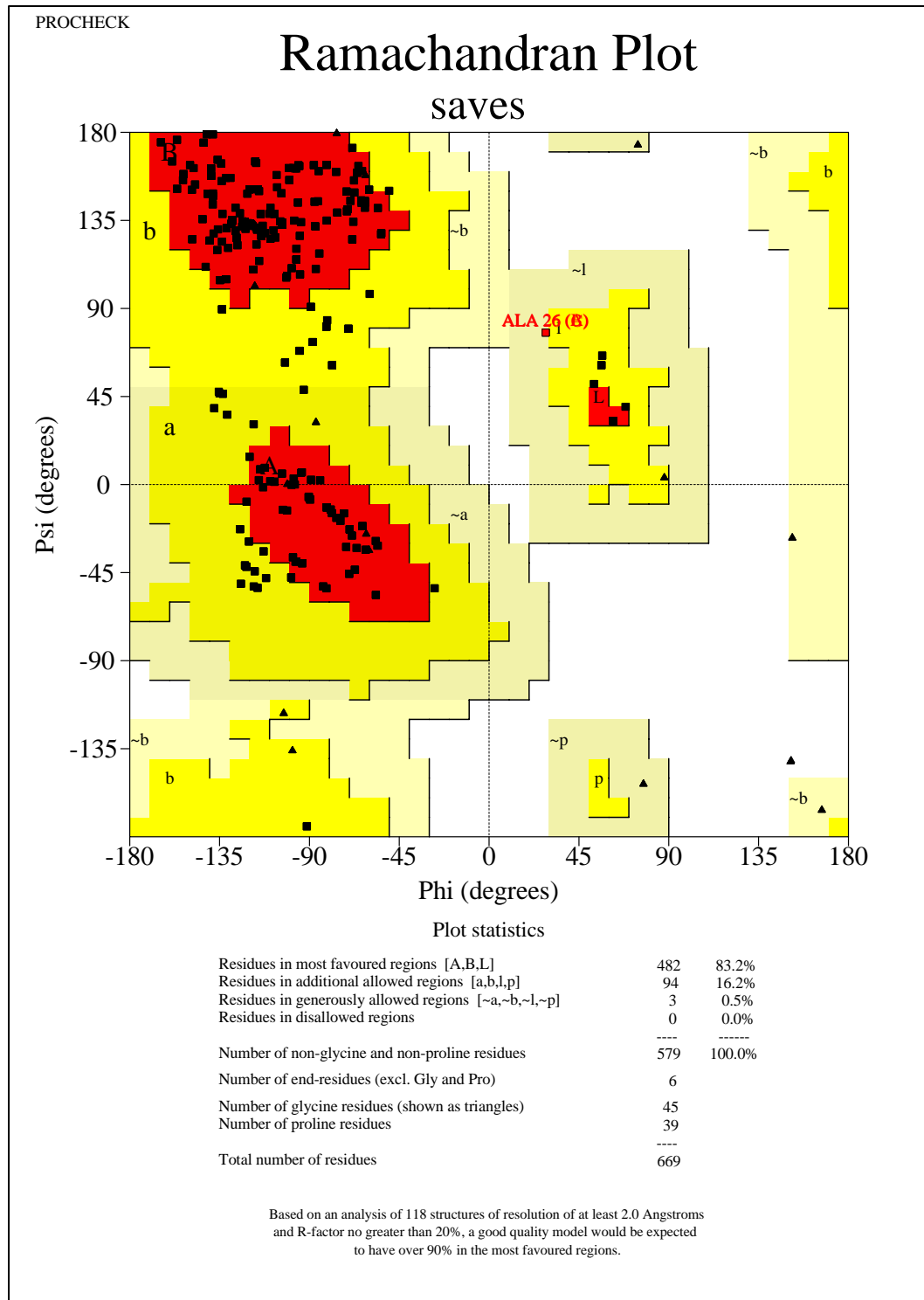


**Supplementary Figure 1(D):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.617(Delta) variant (EPI\_ISL\_1360328)



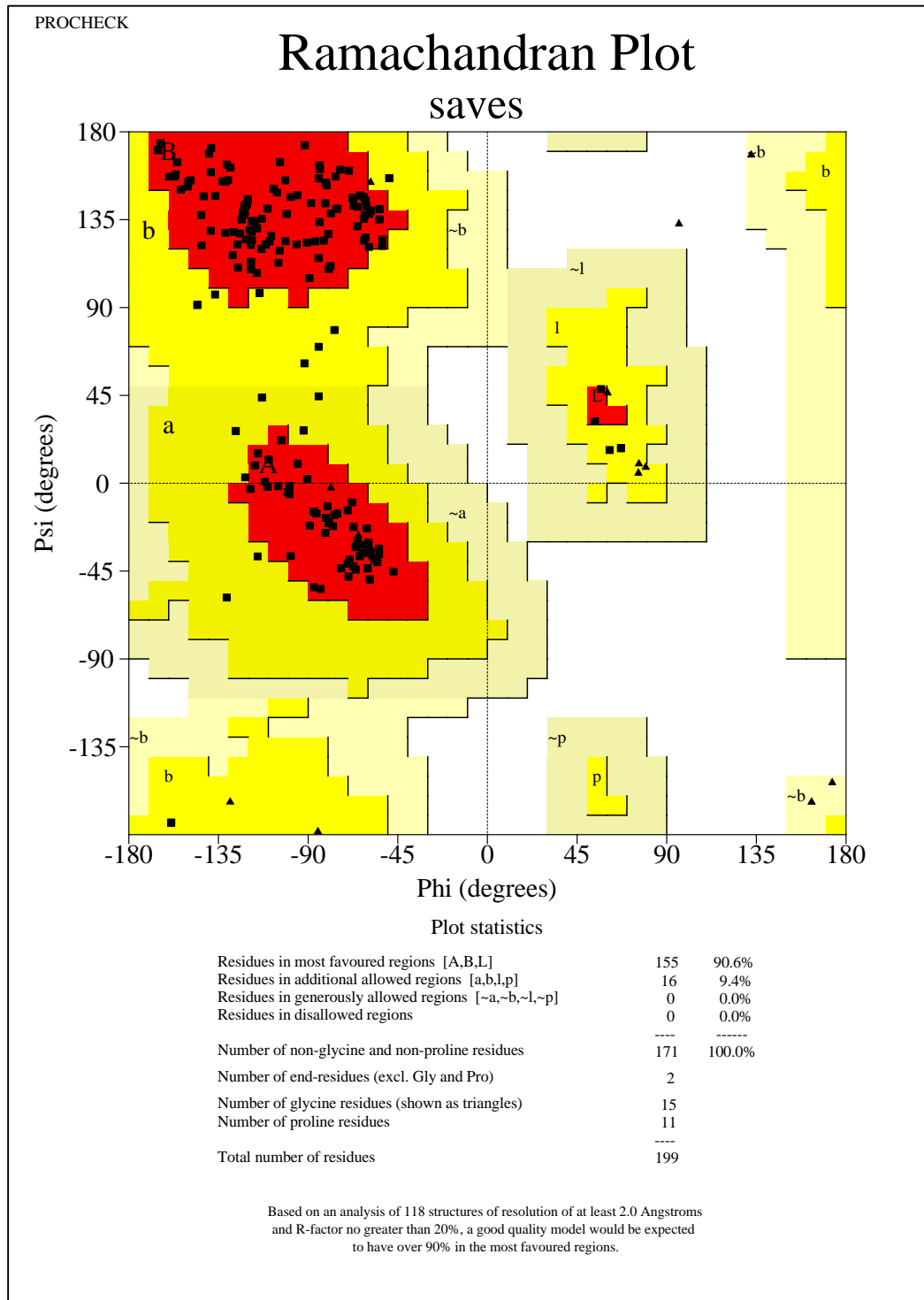
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**Supplementary Figure 1(E):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.1.529(Omicron) variant (EPI\_ISL\_6640917)

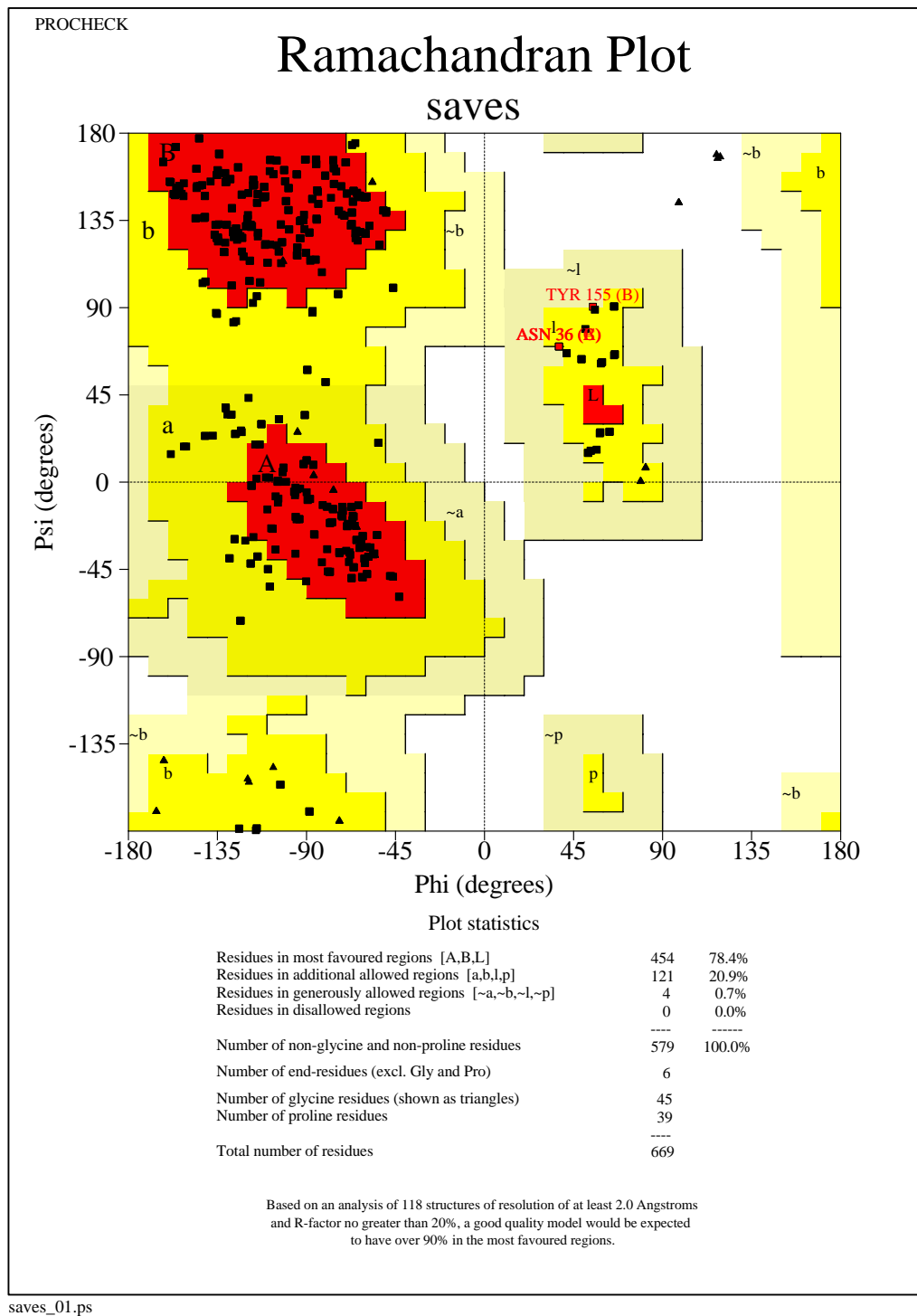


**Supplementary Figure 1(F):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 C.37(Lambda) variant (EPI\_ISL\_1111334)

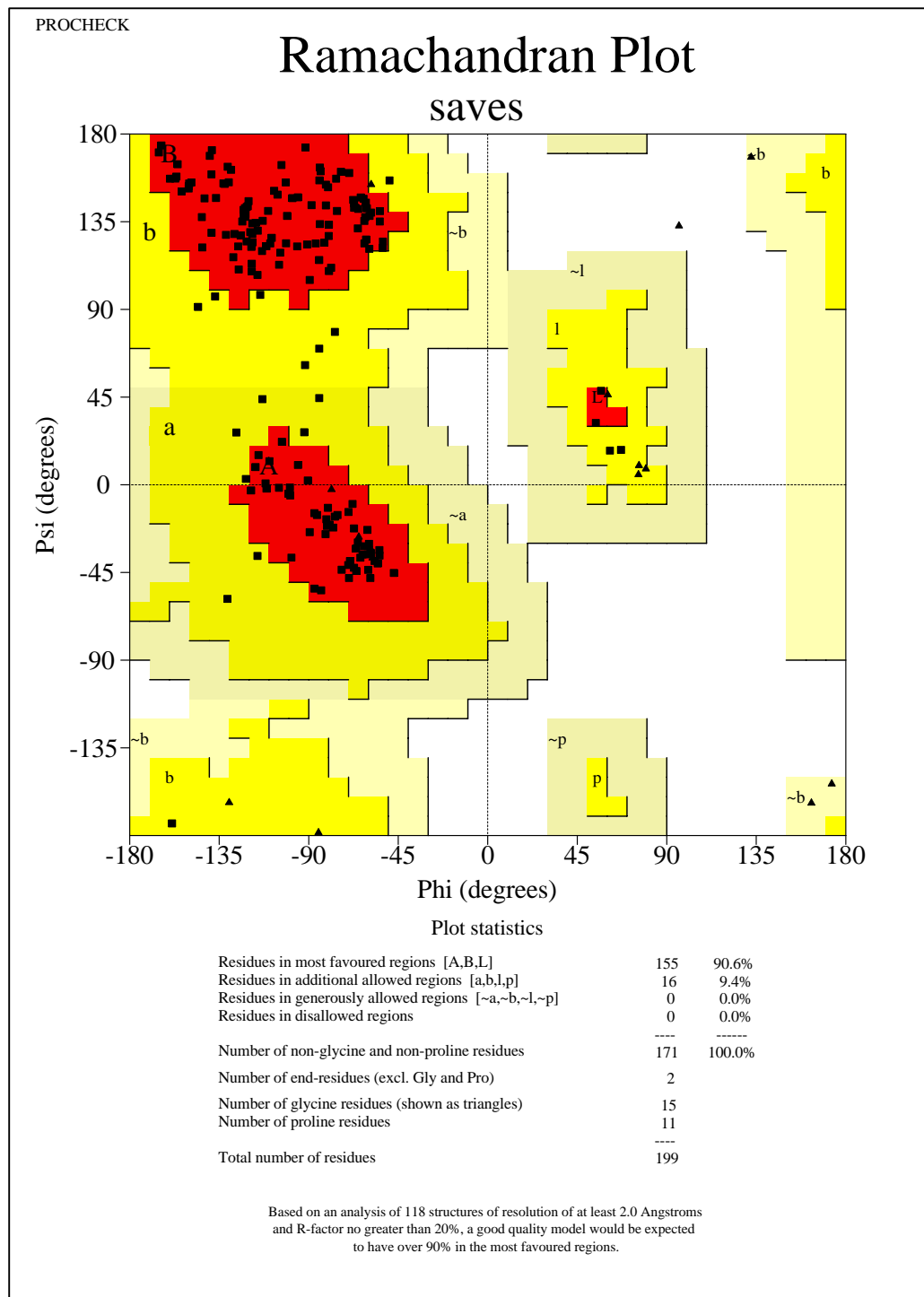




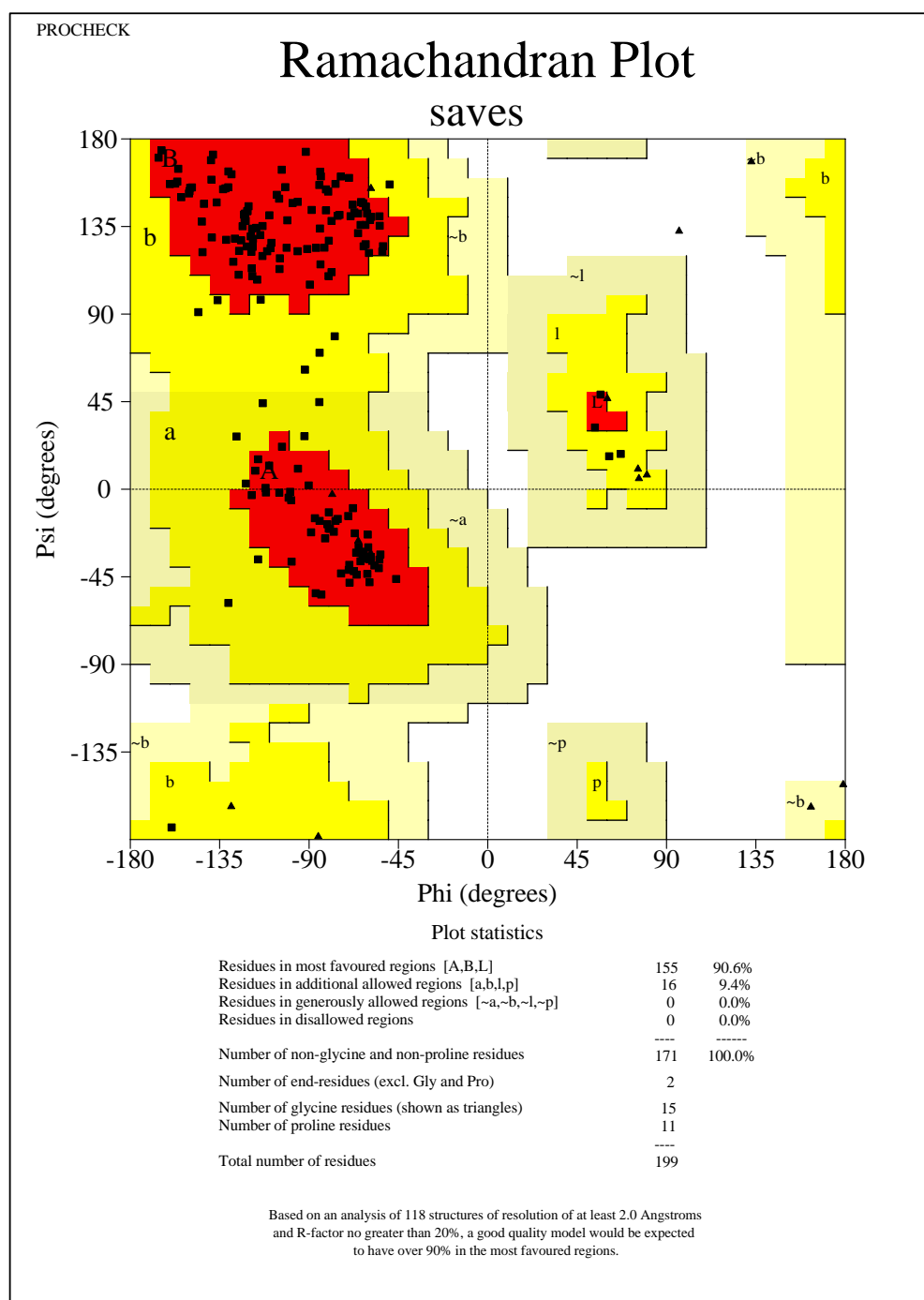
**Supplementary Figure 1(G):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.621(Mu) variant (EPI\_ISL\_3369952)



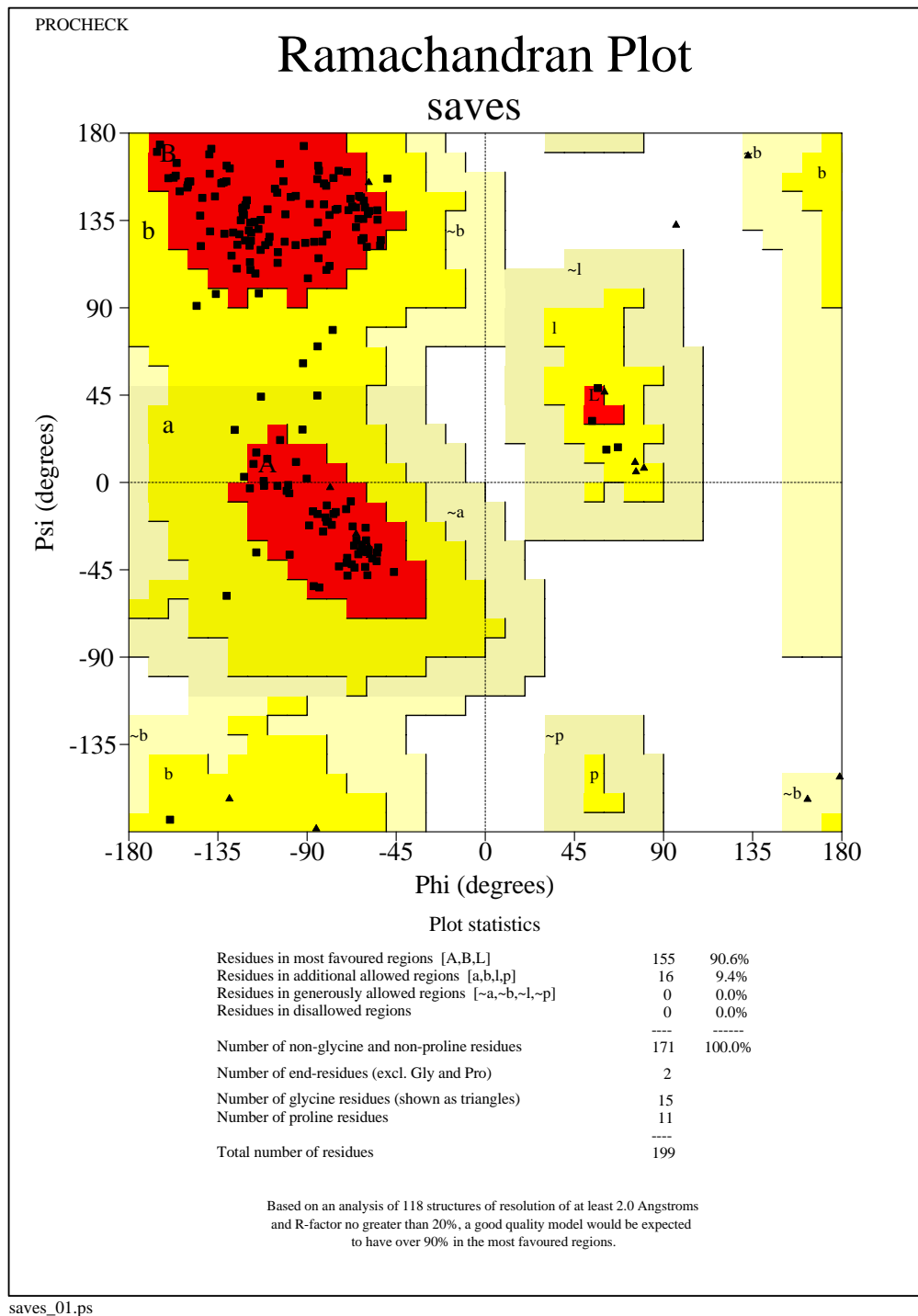
**Supplementary Figure 1(H):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.427/B.1.429(Epsilon) variant (EPI\_ISL\_648527)



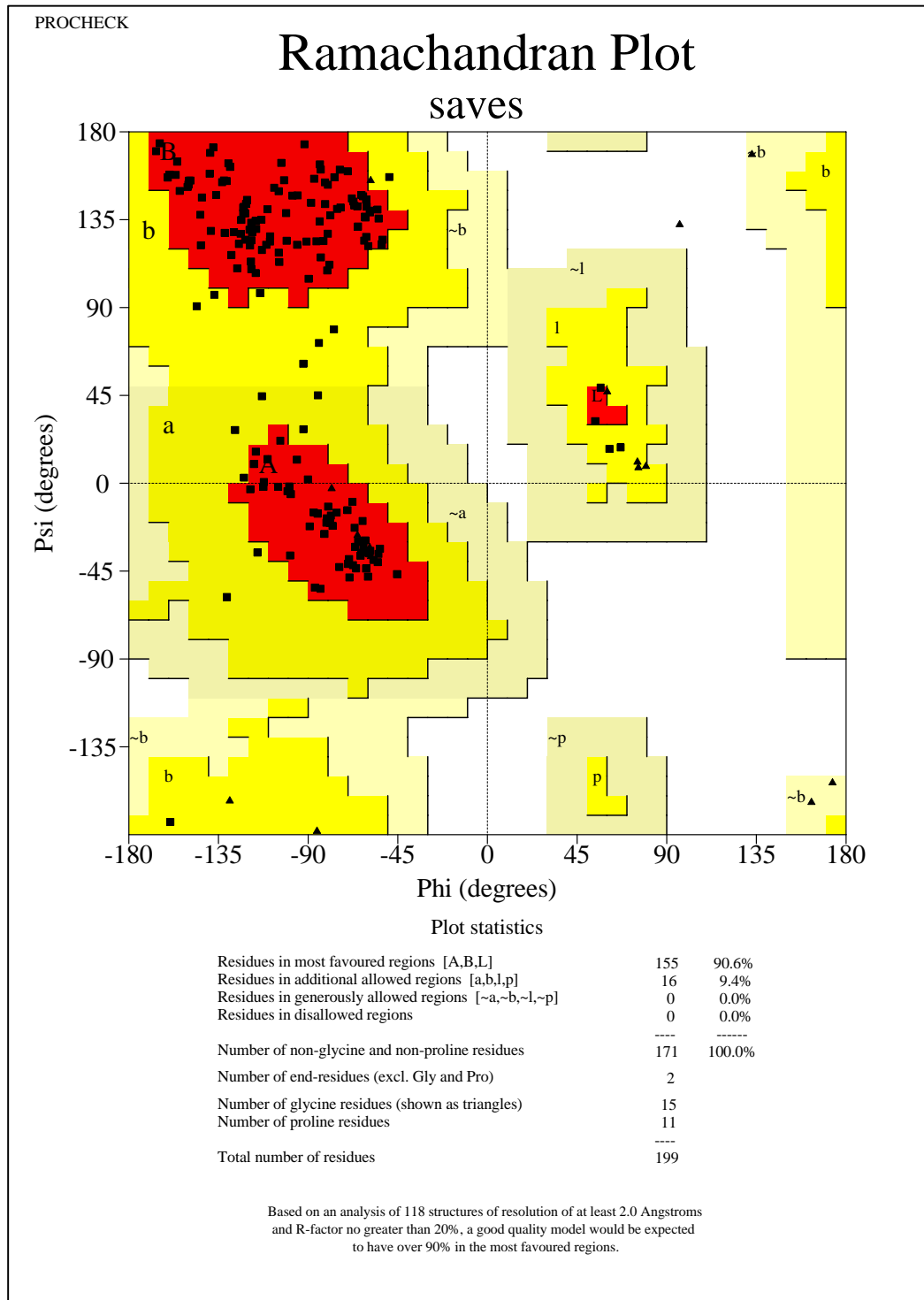
**Supplementary Figure 1(I):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.1.519 variant (EPI\_ISL\_721617)



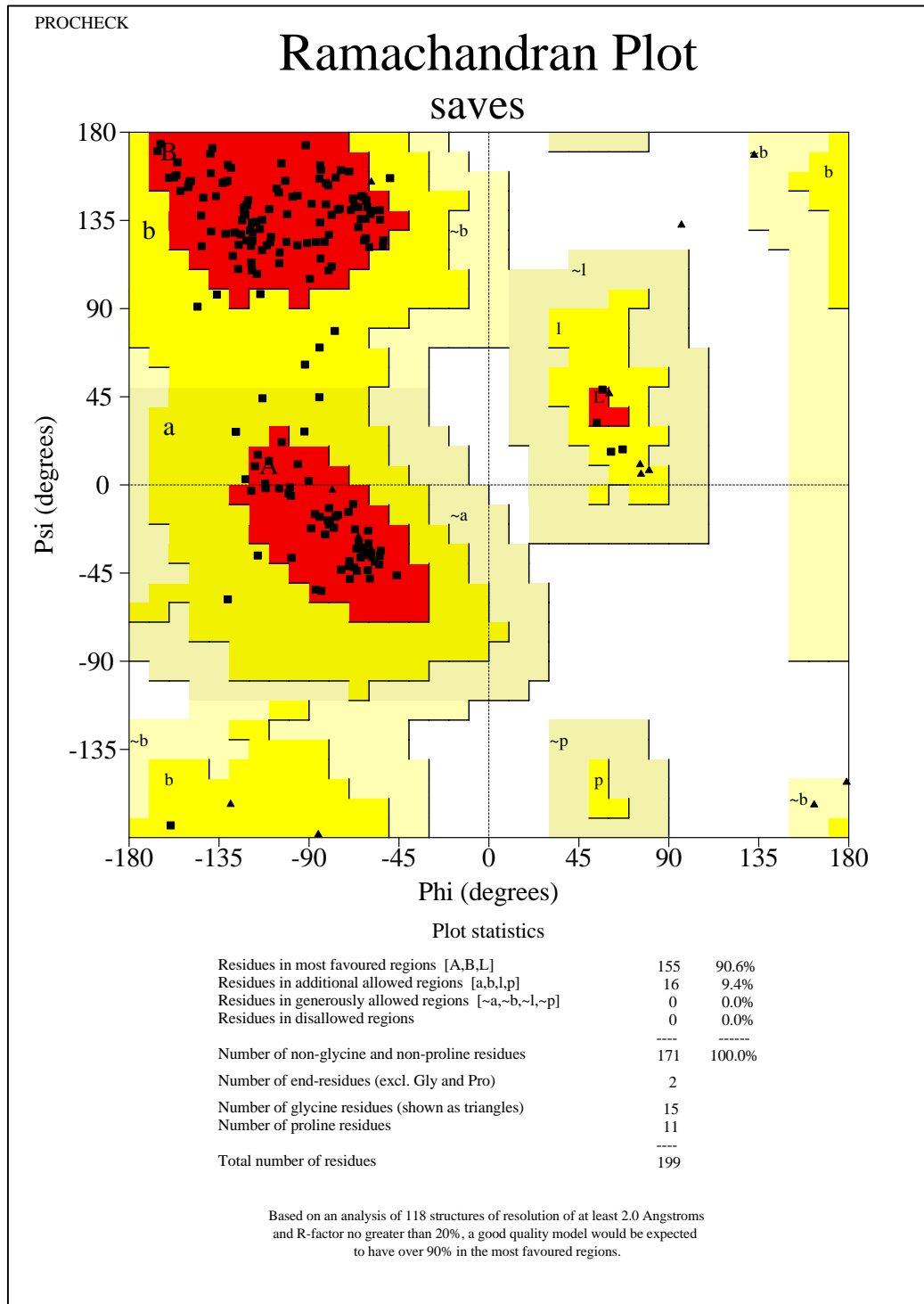
**Supplementary Figure 1(J):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 R.1 variant (EPI\_ISL\_736897)



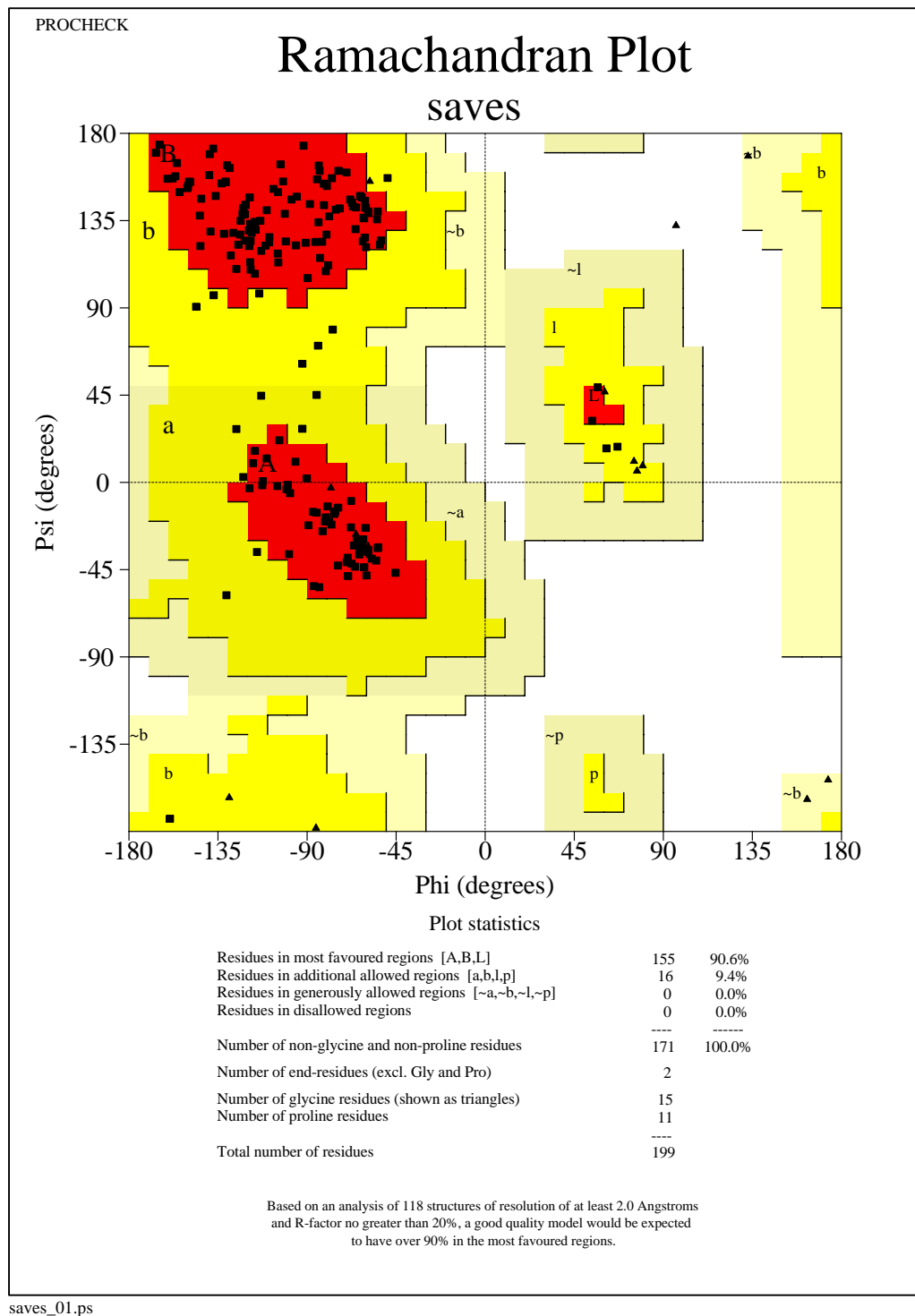
**Supplementary Figure 1(K):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.525(Eta) variant (EPI\_ISL\_760883)



**Supplementary Figure 1(L):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.214.2 variant (EPI\_ISL\_760951)

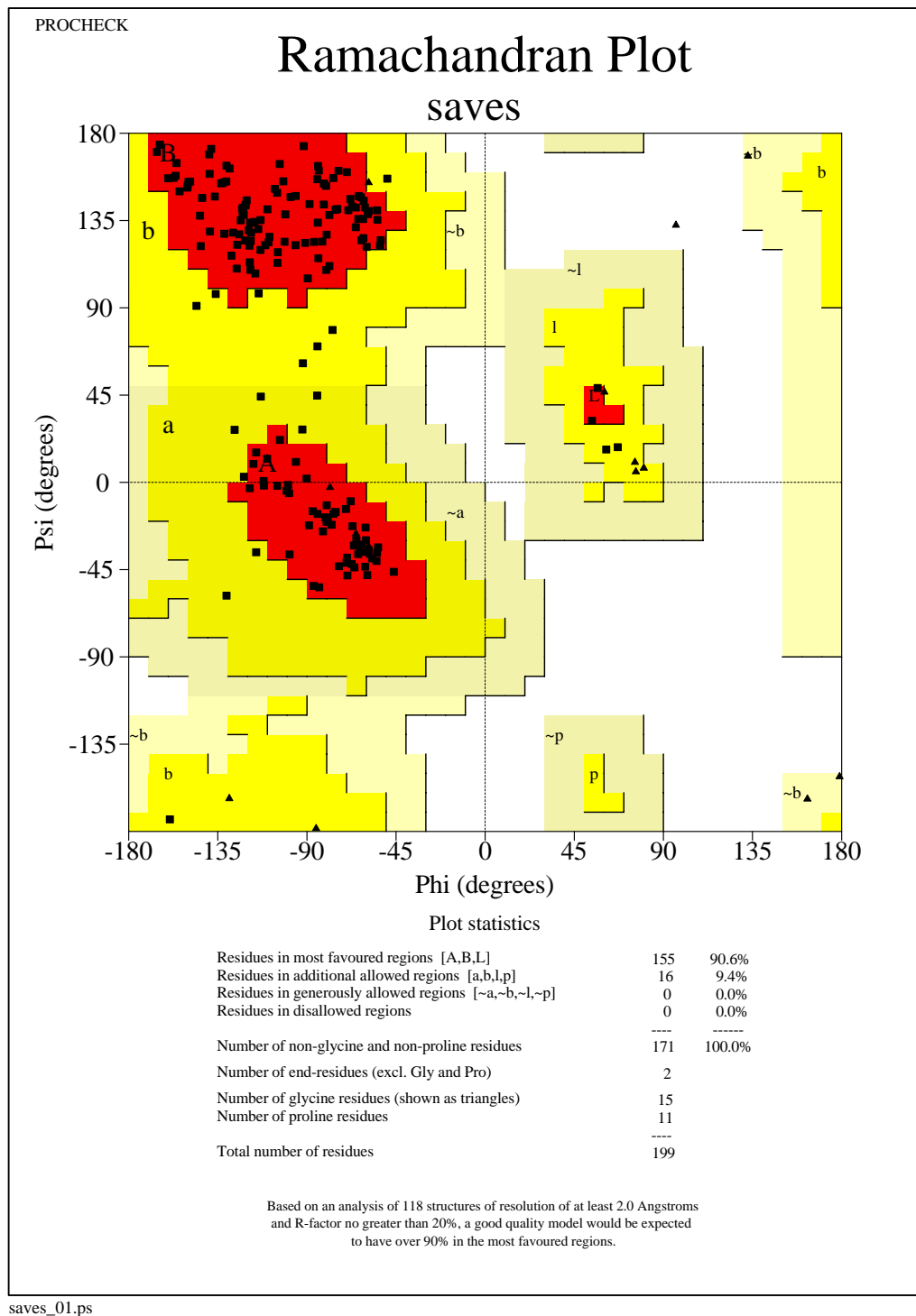


**Supplementary Figure 1(M):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.526(Lota) variant (EPI\_ISL\_765494)

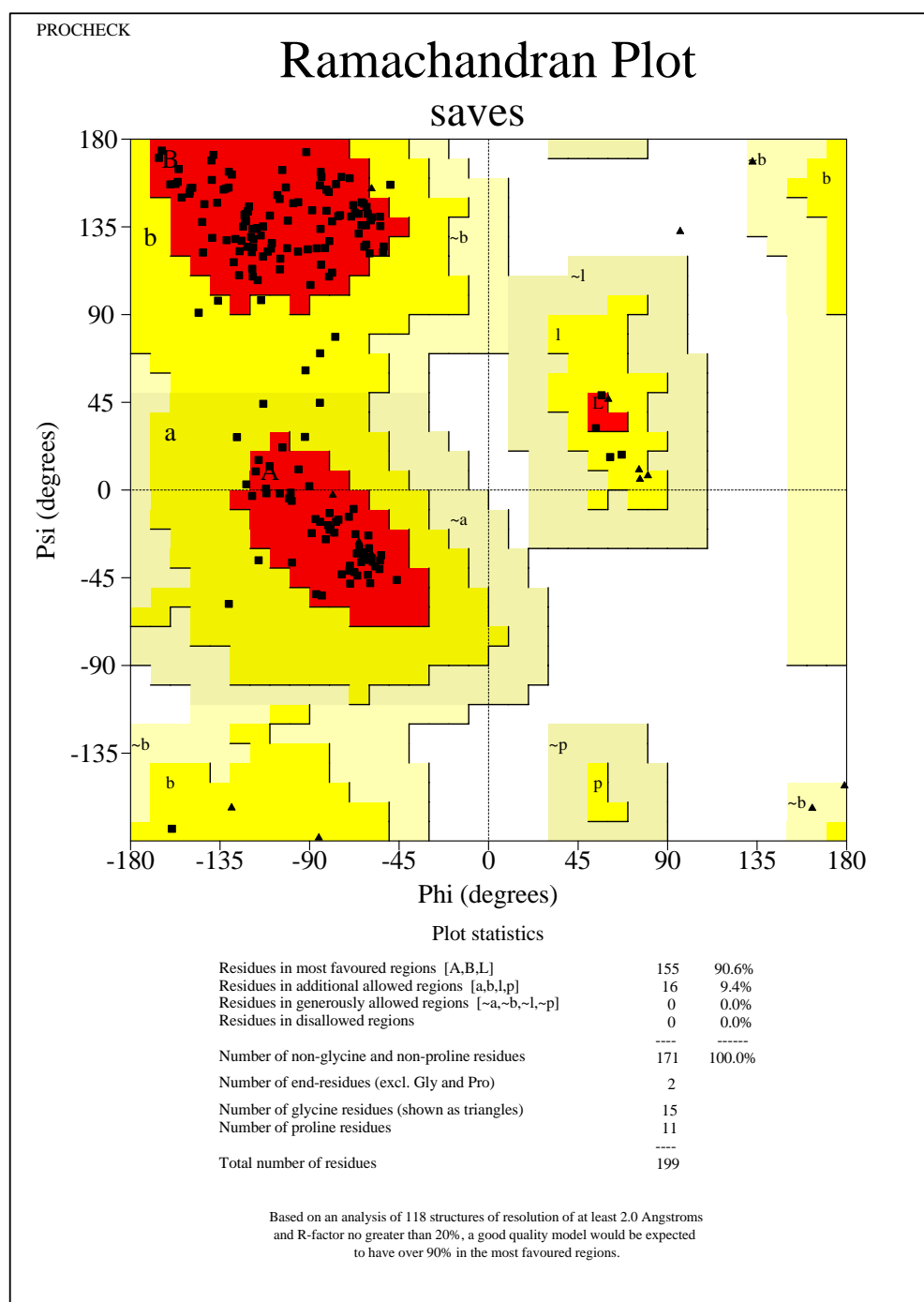


**Supplementary Figure 1(N):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.466.2 variant (EPI\_ISL\_877419)



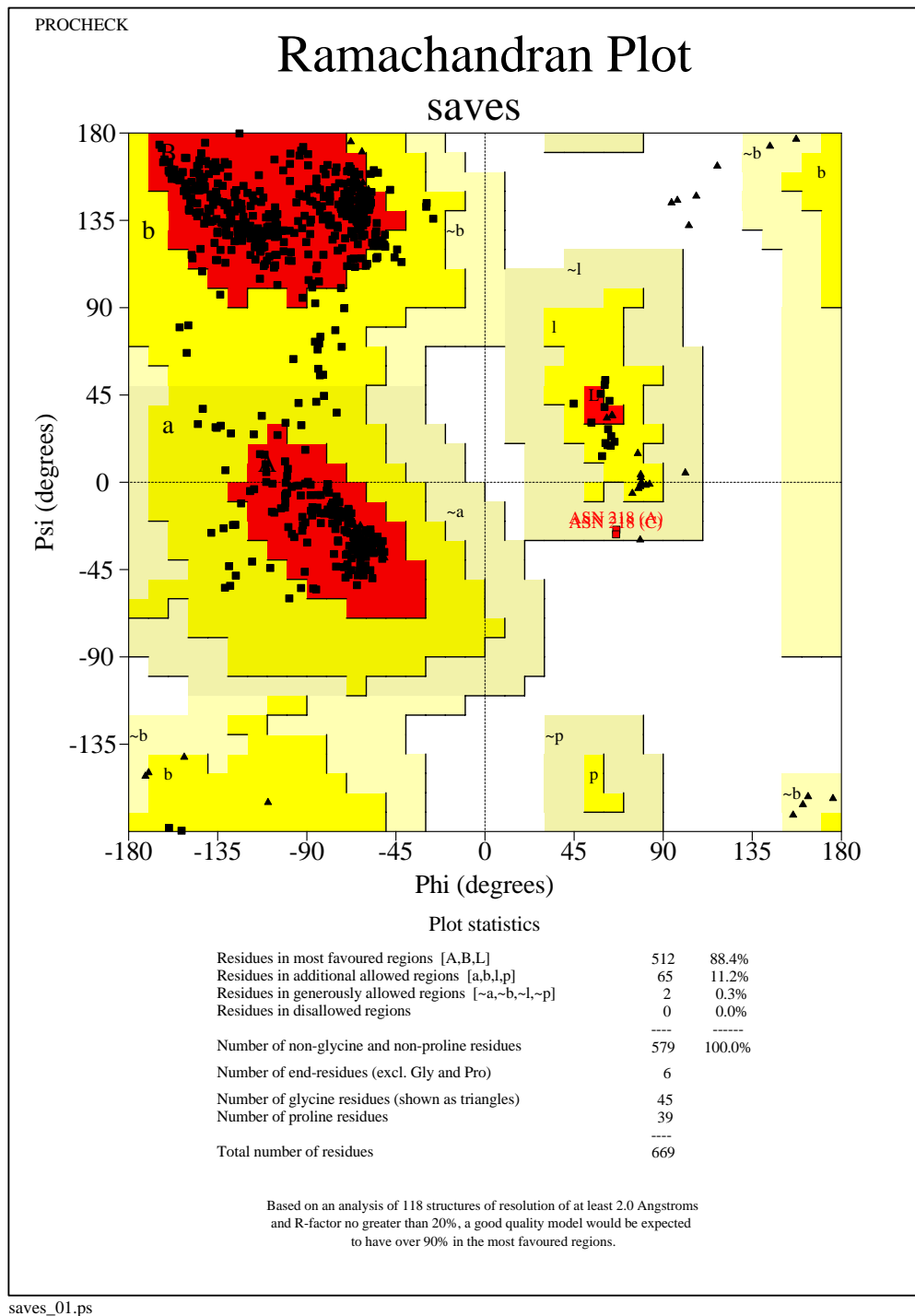


**Supplementary Figure 1(O):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.1.318 variant (EPI\_ISL\_937654)

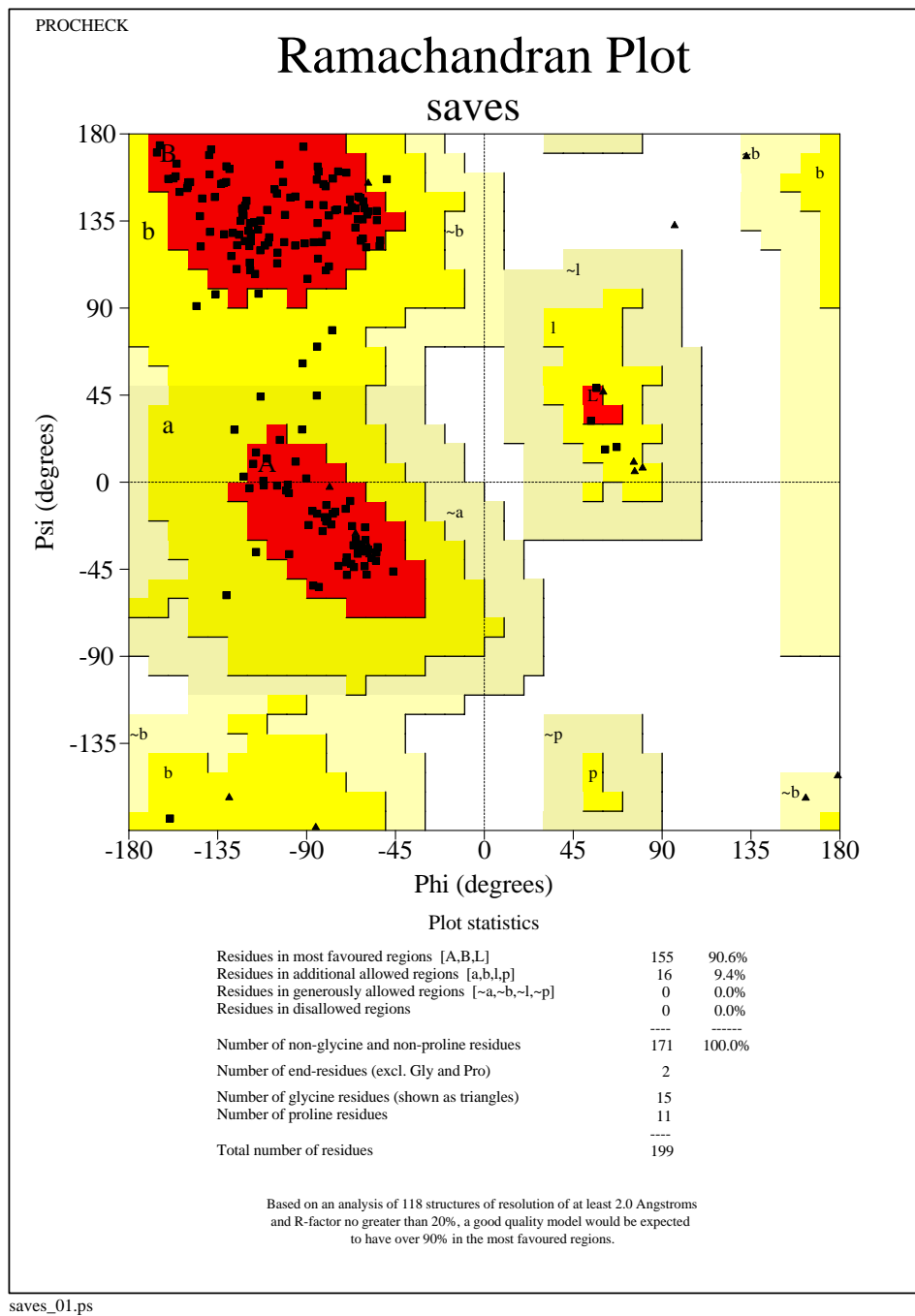


saves\_01.ps

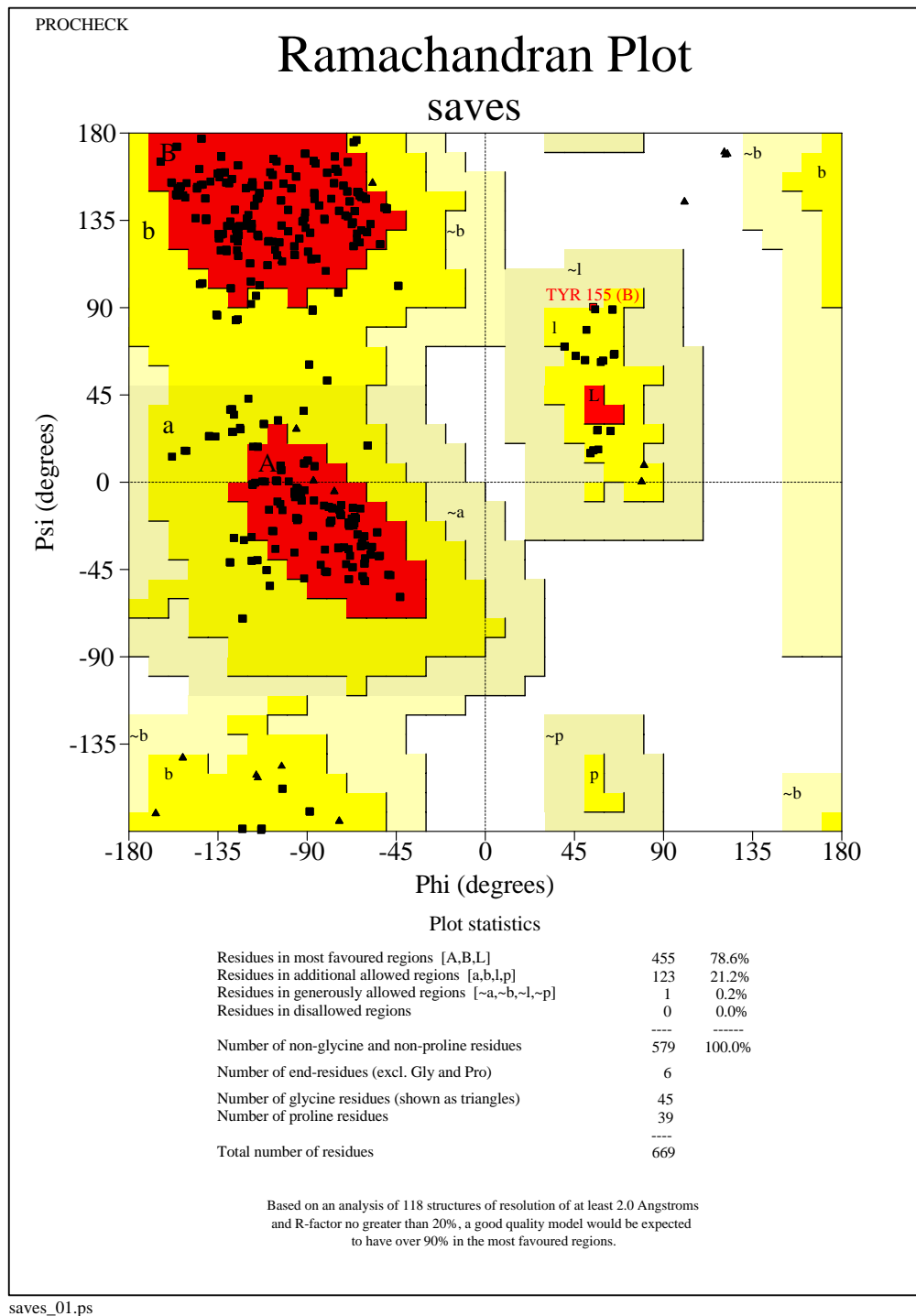
**Supplementary Figure 1(P):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.619 variant (EPI\_ISL\_1150929)



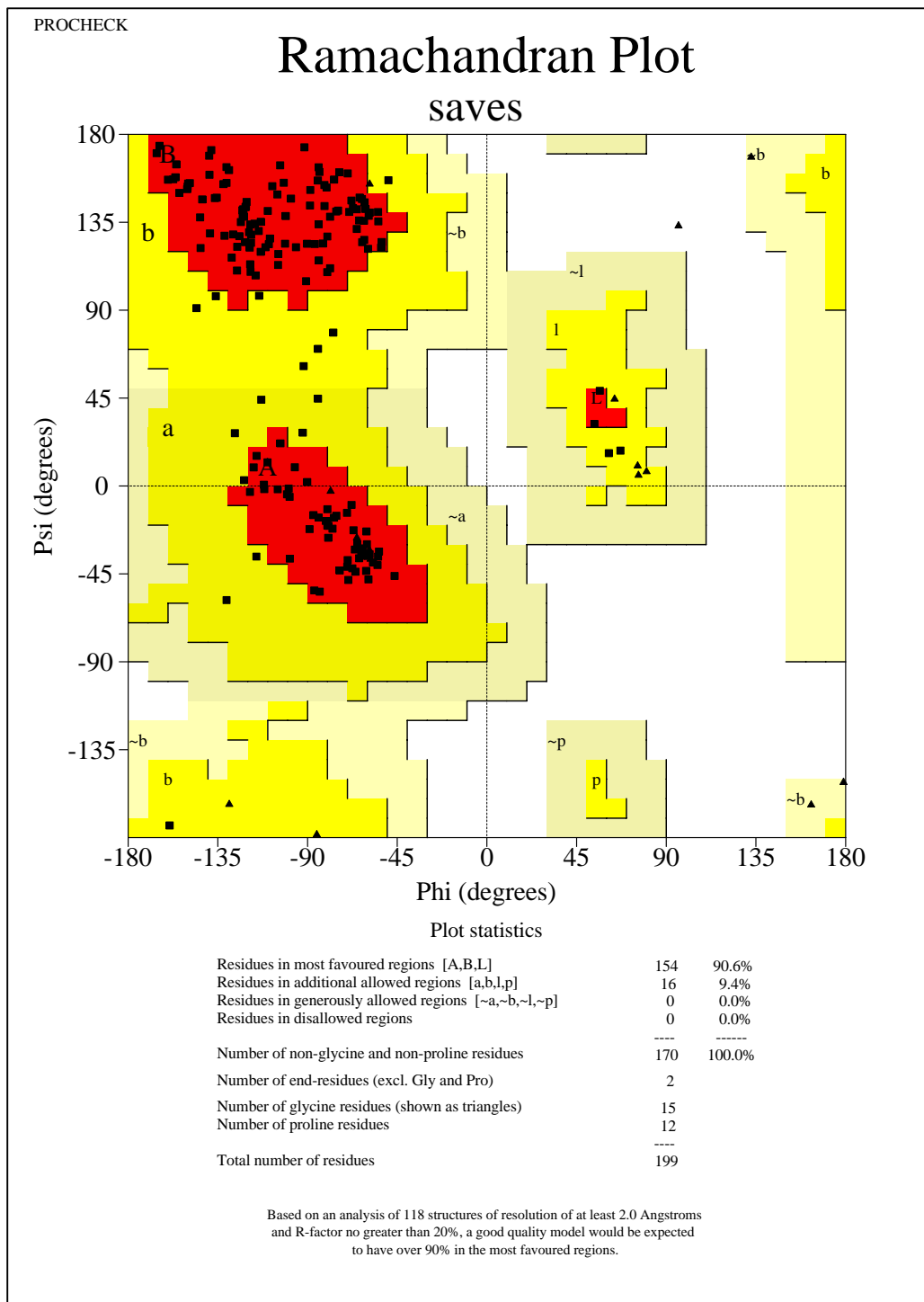
**Supplementary Figure 1(Q):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 C.36.3 variant (EPI\_ISL\_1237137)



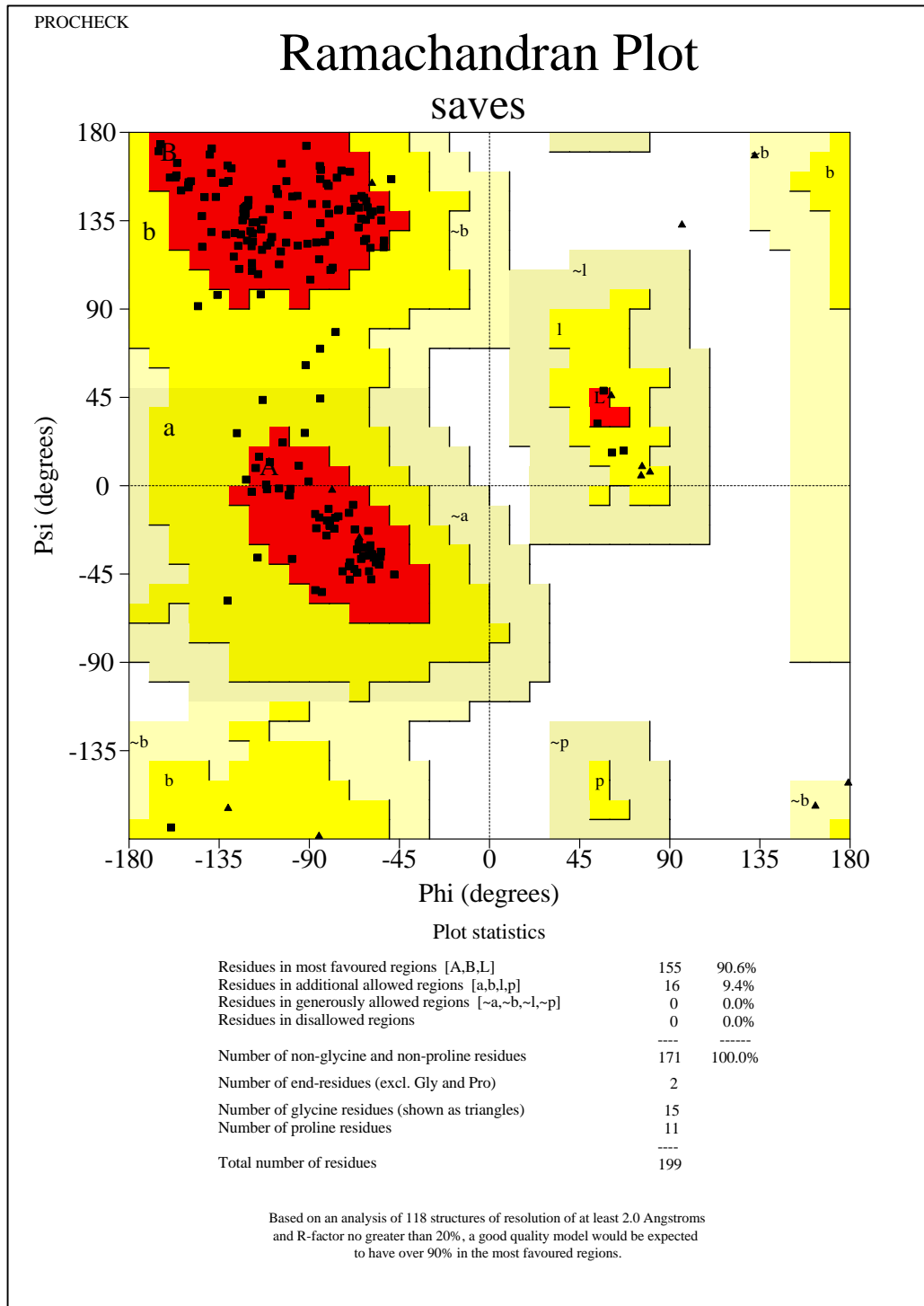
**Supplementary Figure 1(R):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 AT.1 variant (EPI\_ISL\_1259283)



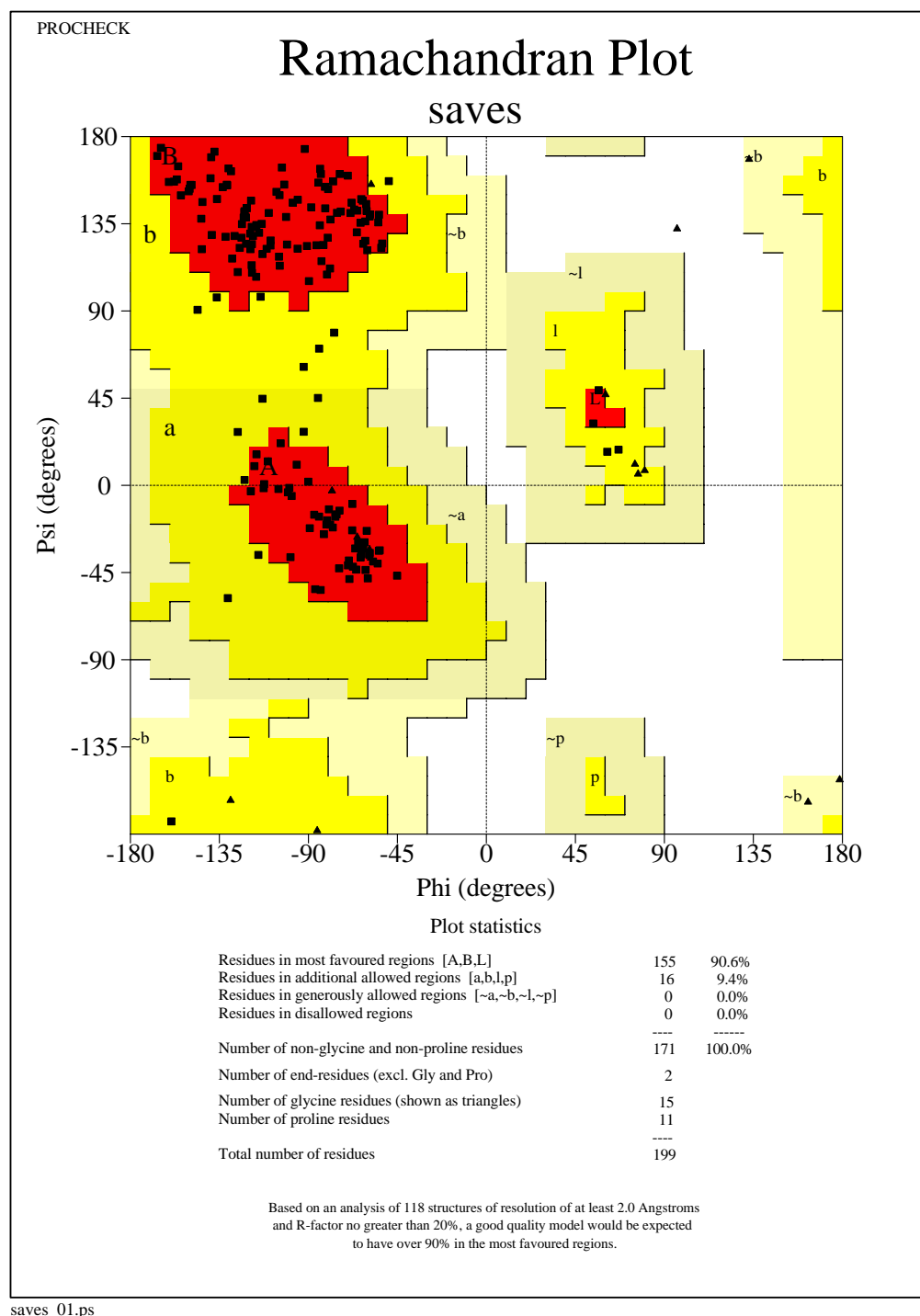
**Supplementary Figure 1(S):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.617.1(Kappa) variant (EPI\_ISL\_1357699)



**Supplementary Figure 1(T):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.1.523 variant (EPI\_ISL\_1448584)

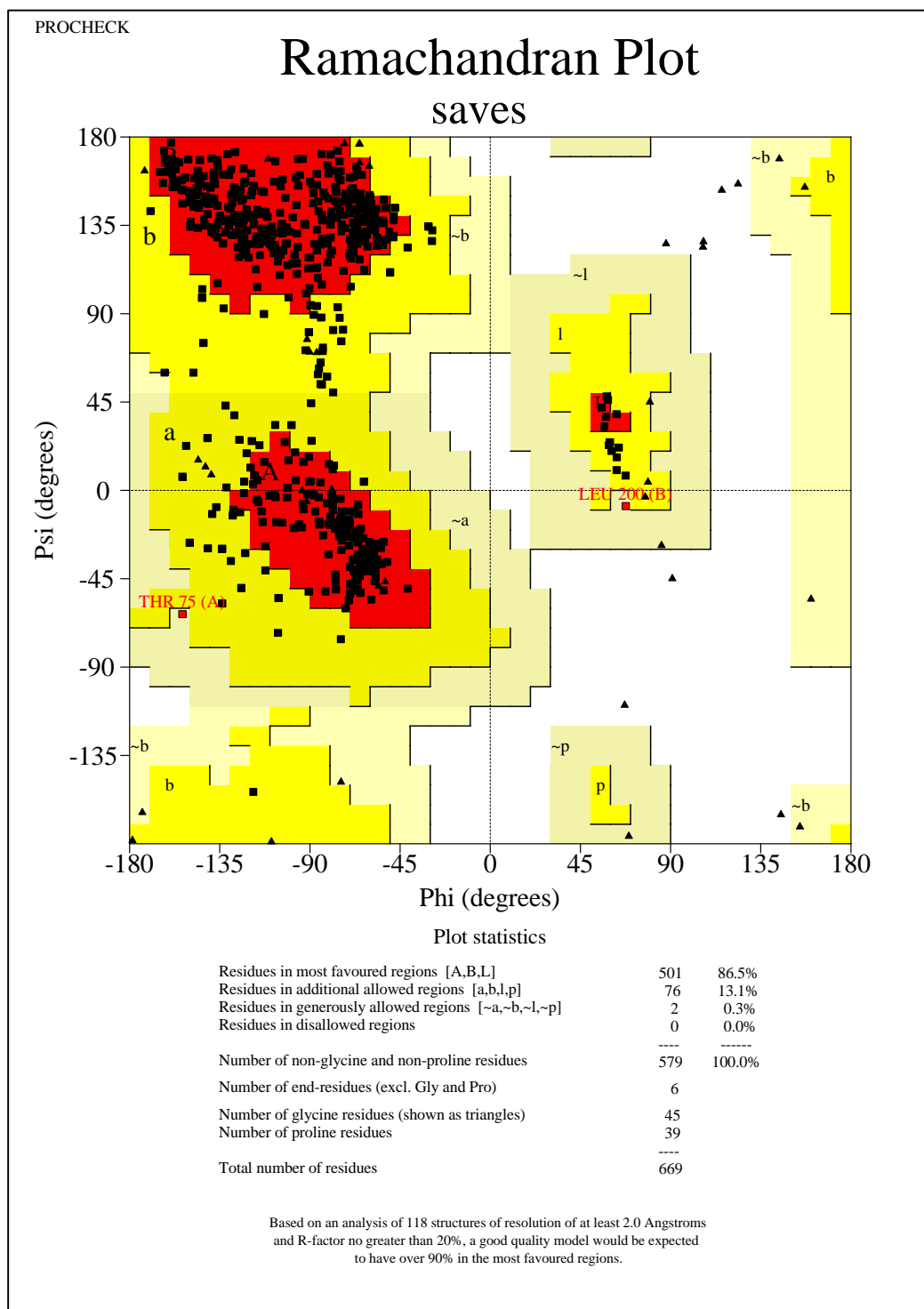


**Supplementary Figure 1(U):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.620 variant (EPI\_ISL\_1579527)

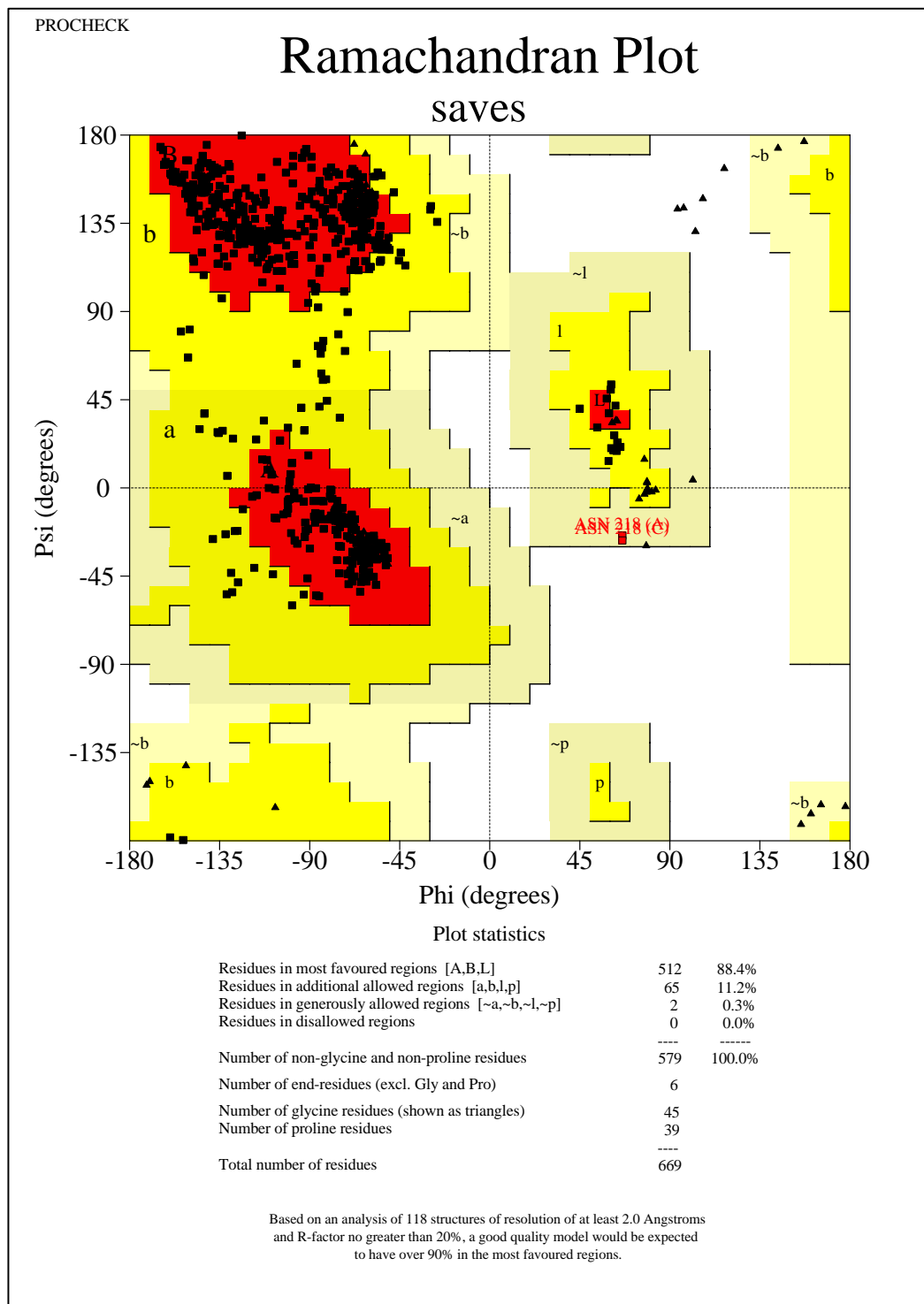


**Supplementary Figure 1(V):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 AV.1 variant (EPI\_ISL\_1595332)



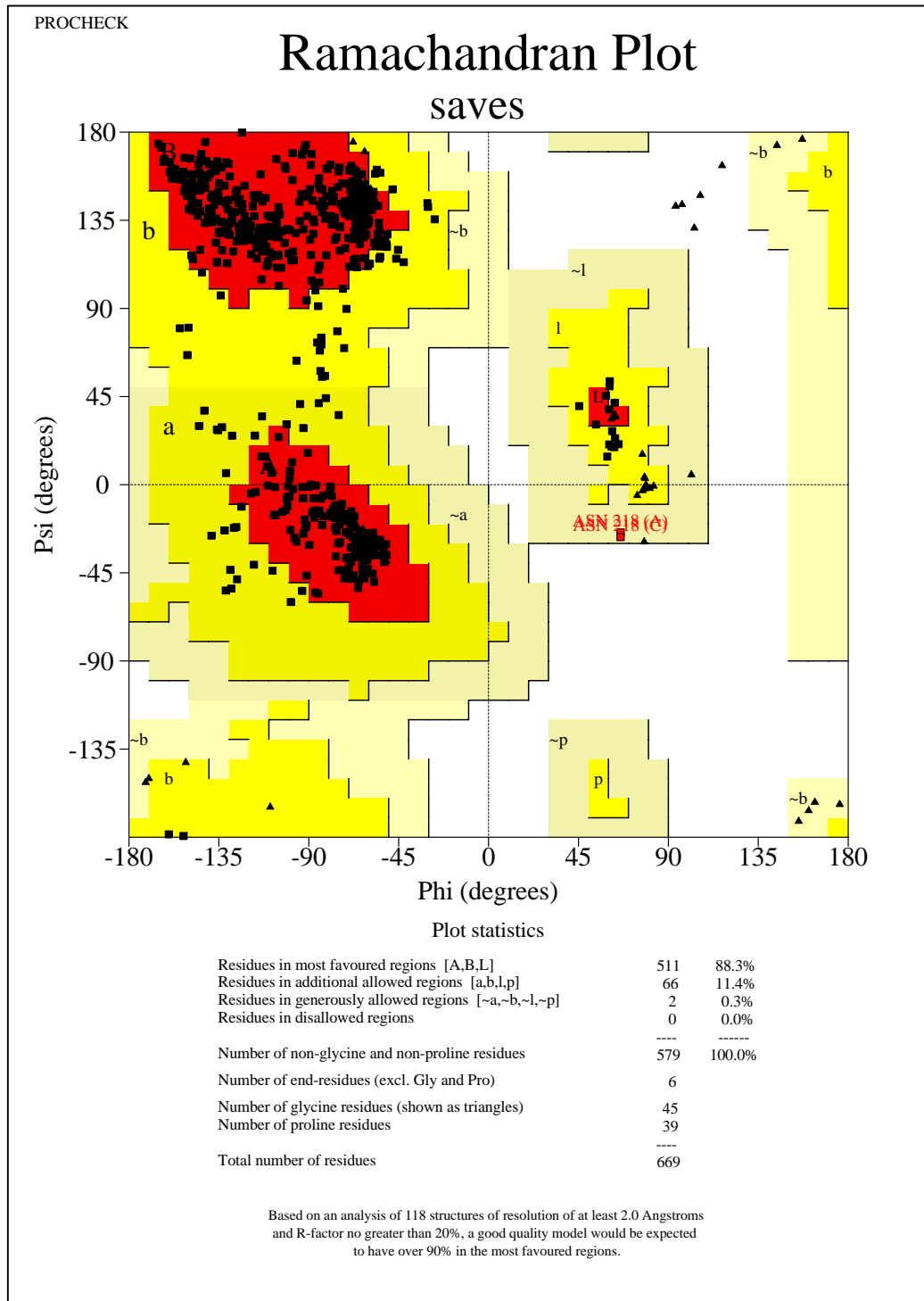


**Supplementary Figure 1(W):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.630 variant (EPI\_ISL\_3045385)



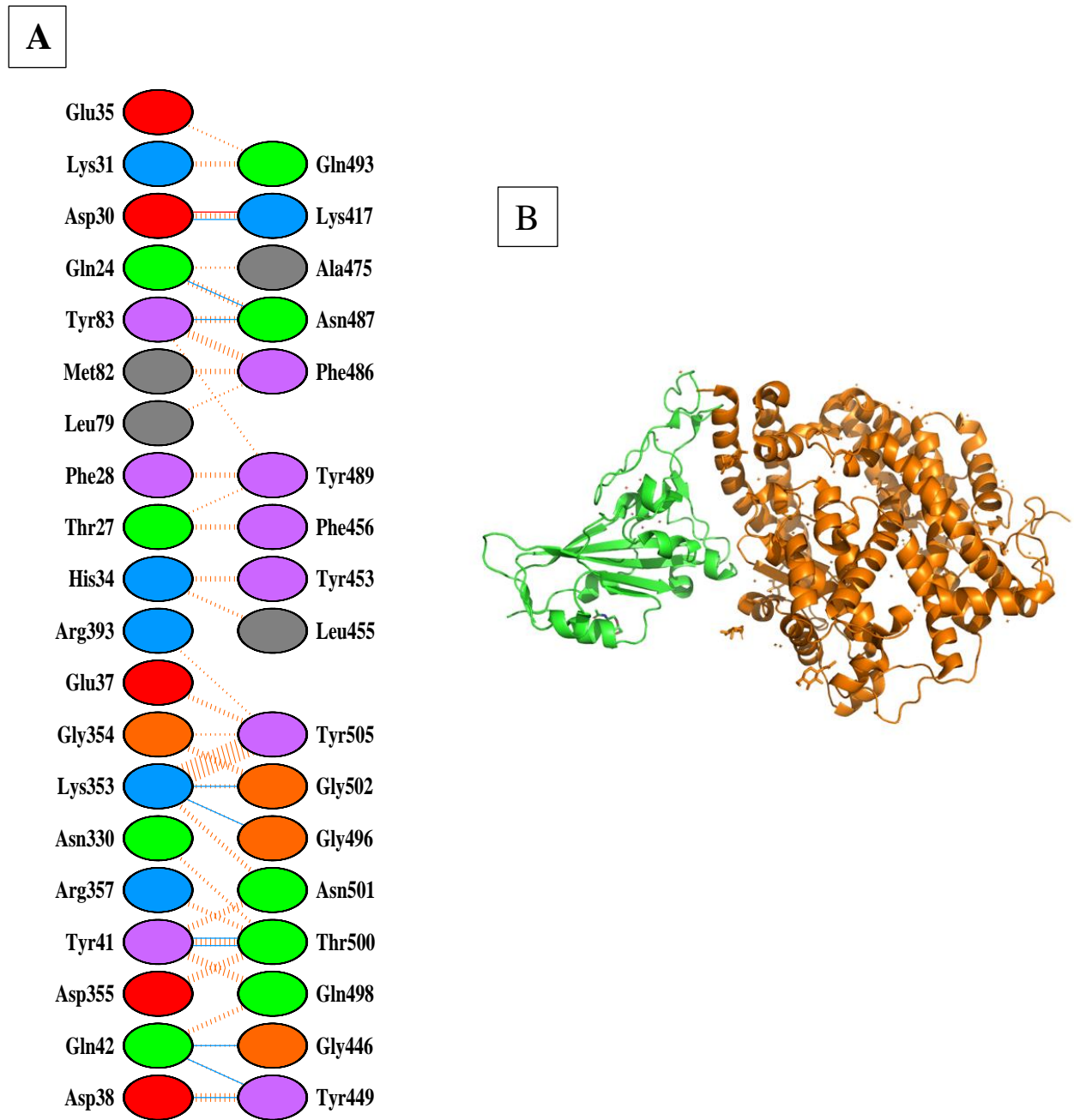
saves\_01.ps

**Supplementary Figure 1(X):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 C.1.2 variant (EPI\_ISL\_3447714)

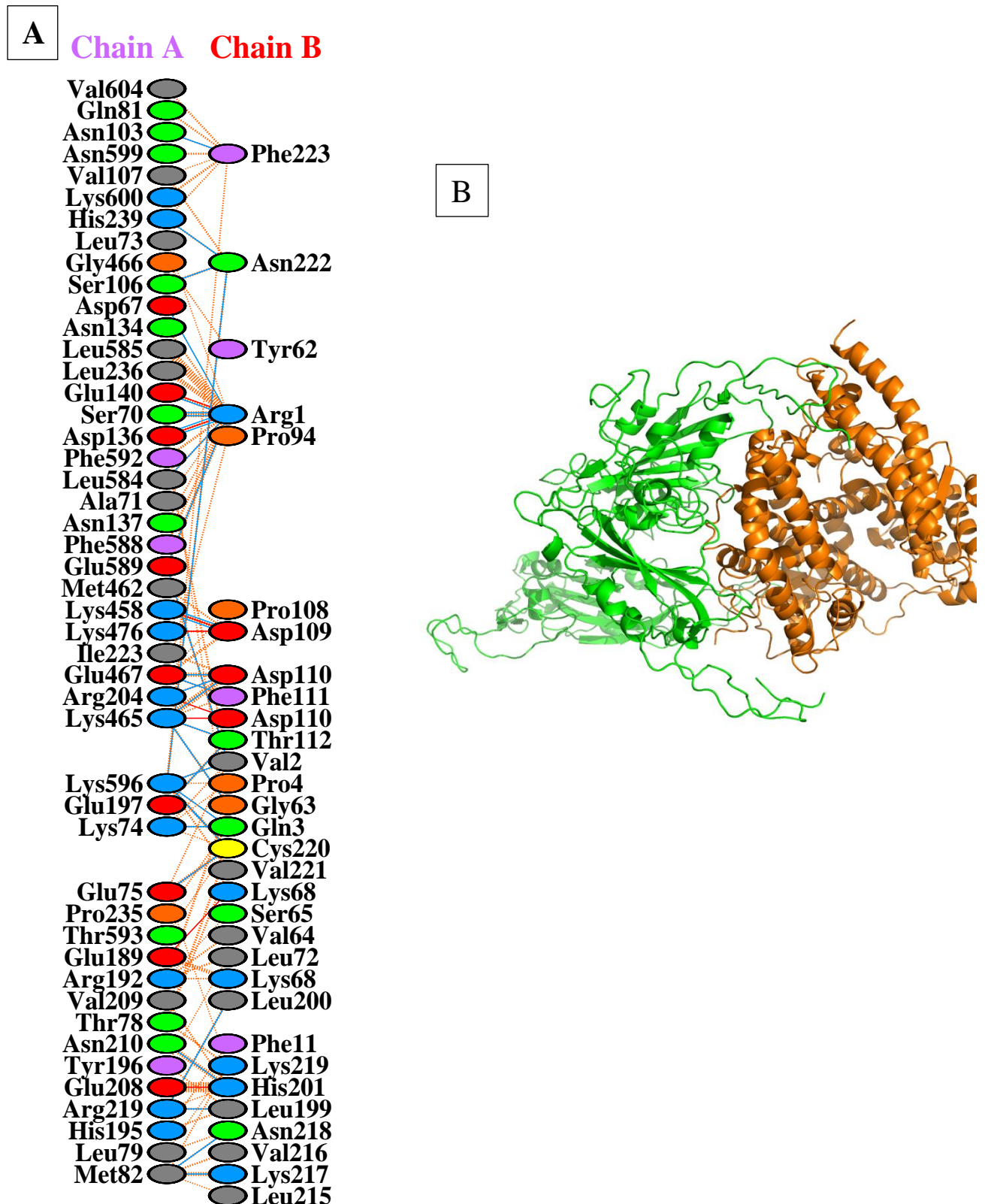


saves\_01.ps

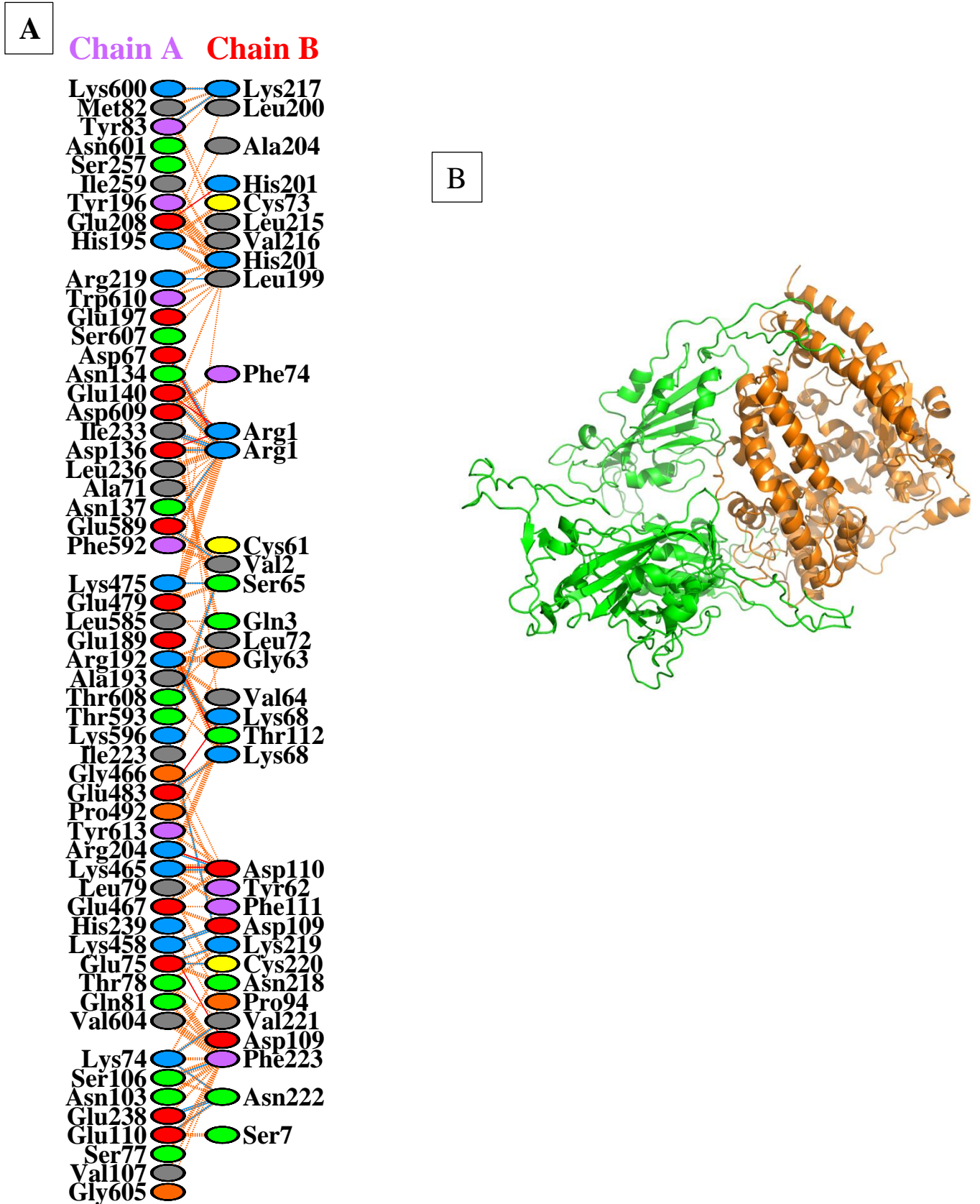
**Supplementary Figure 1(Y):** The PROCHECK Ramachandran plot for the validation of the 3D model of Spike RBD of SARS-CoV-2 B.1.640 variant (EPI\_ISL\_5592661)



**Supplementary Figure 2A: Protein–protein docking representation of hACE2 and RBD of WIV04(EPI\_ISL\_402124)**. (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

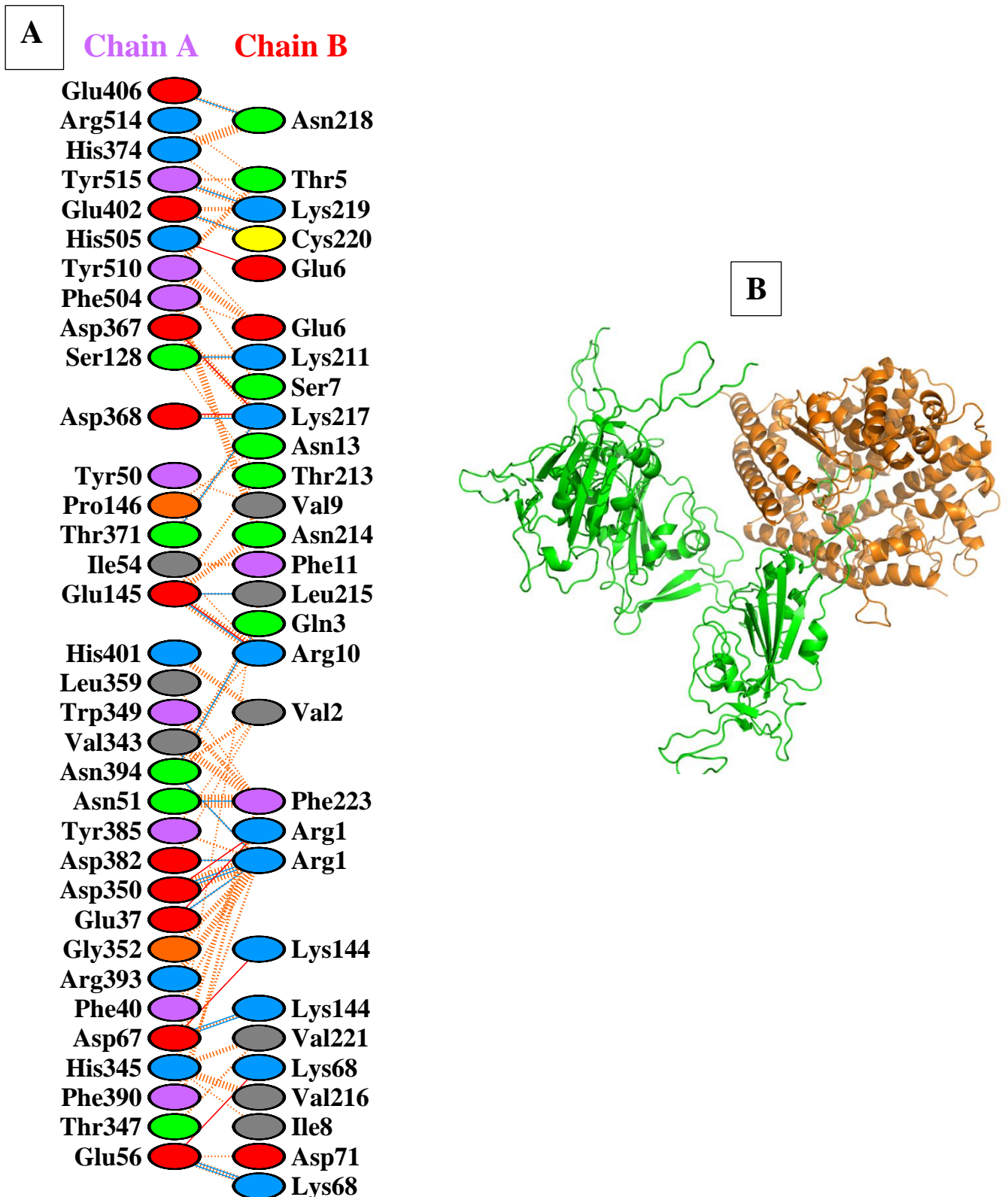


**Supplementary Figure 2B: Protein-protein docking representation of hACE2 and RBD of B.1.1.7(Alpha) (EPI\_ISL\_596982).** (A) The interaction representation, which includes hydrogen ( ——— ), salt bridges ( ——— ), and non-bonded ( ||||| ) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

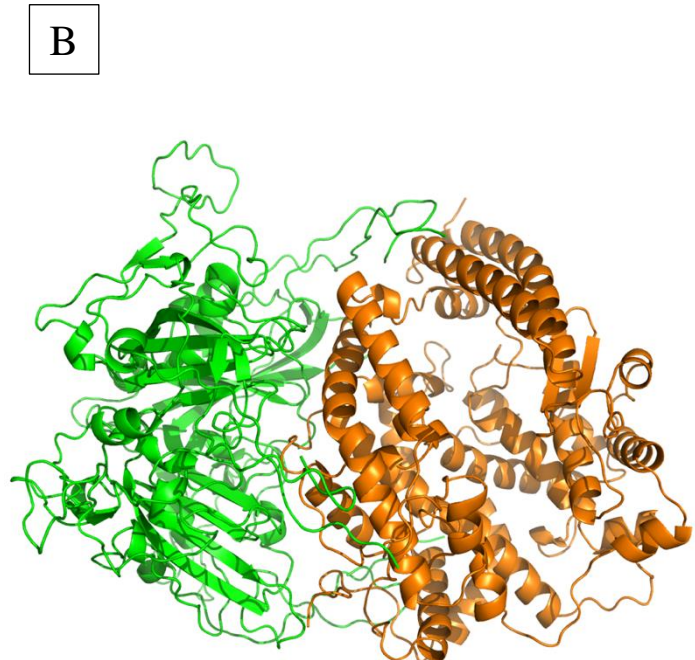
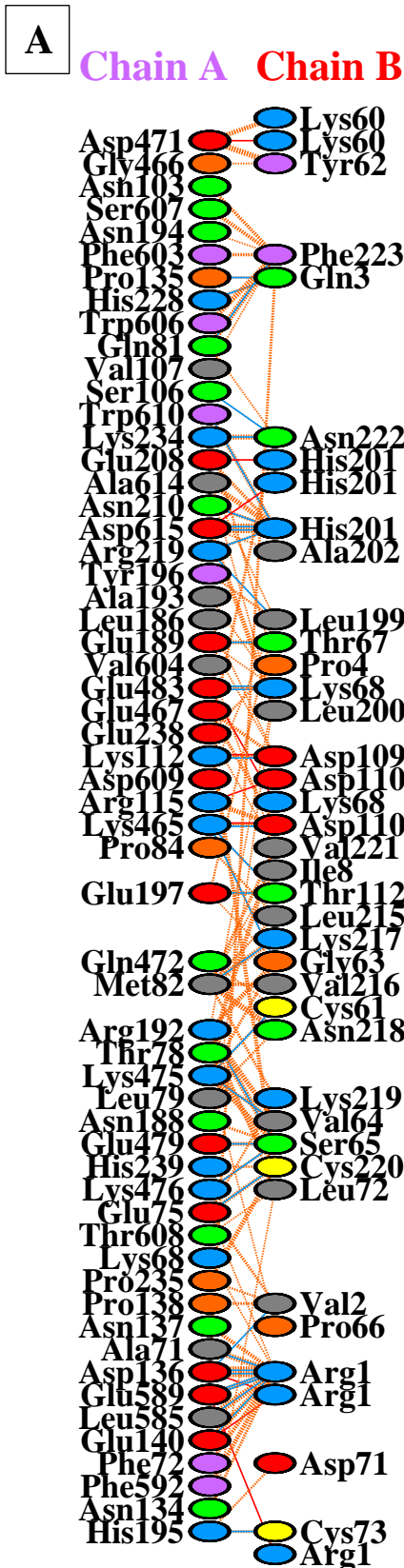


**Supplementary Figure 2C: Protein–protein docking representation of hACE2 and RBD of B.1.351(Beta) (EPI\_ISL\_660629).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



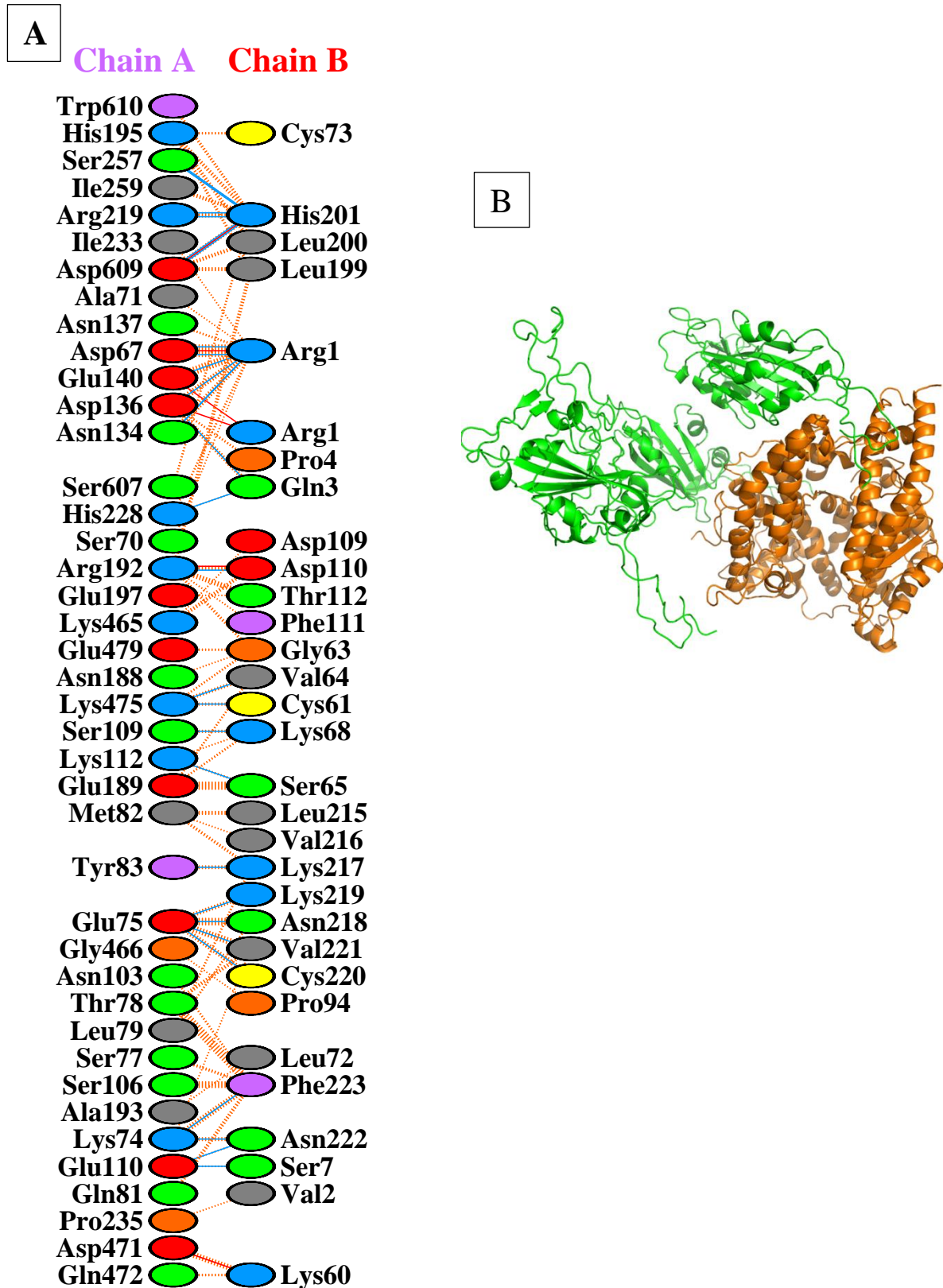


**Supplementary Figure 2D: Protein–protein docking representation of hACE2 and RBD of B.1.1.28.1 (Gamma) (EPI\_ISL\_811149).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

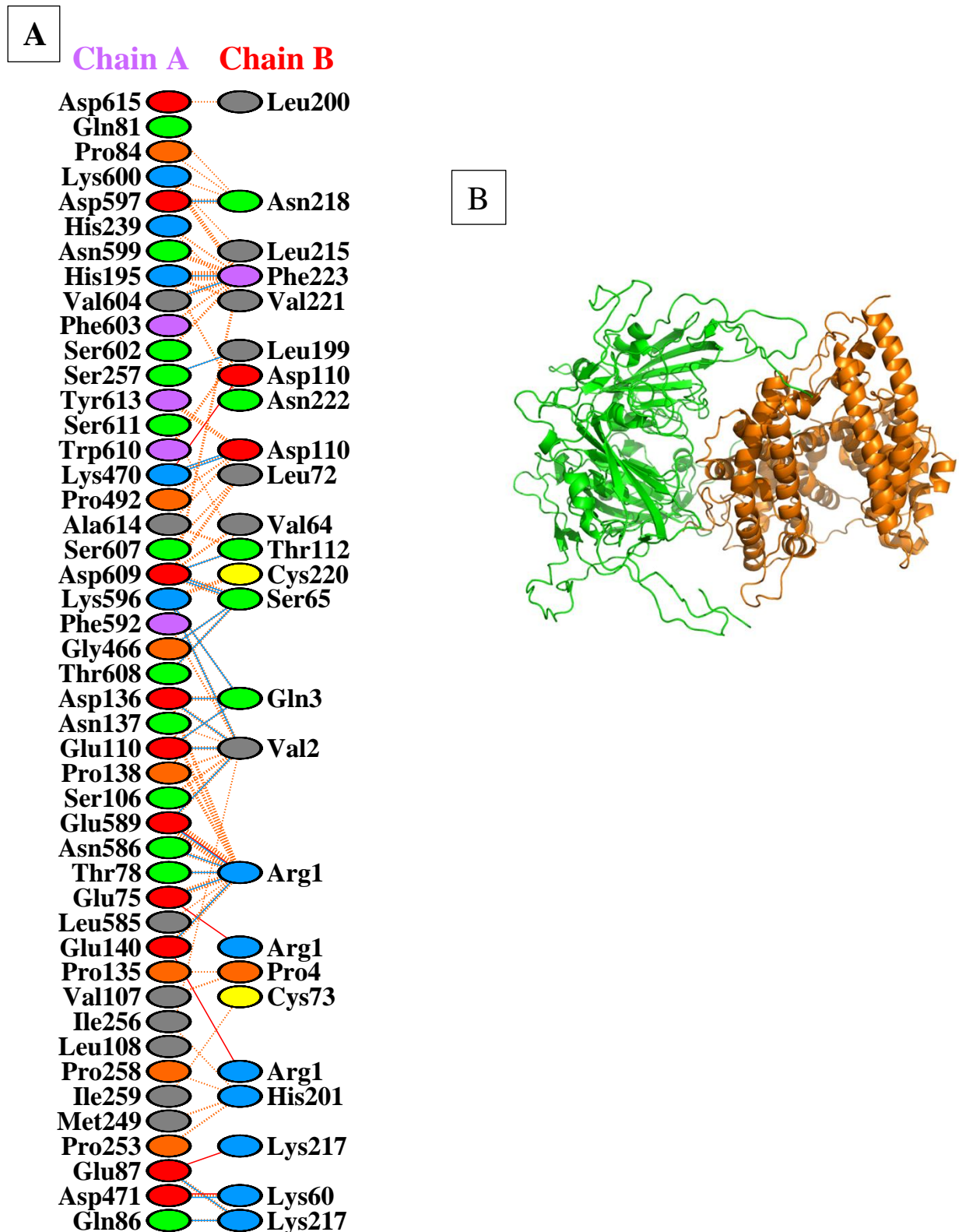


**Supplementary Figure 2E: Protein–protein docking representation of hACE2 and RBD of B.1.617(Delta) (EPI\_ISL\_1360328).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

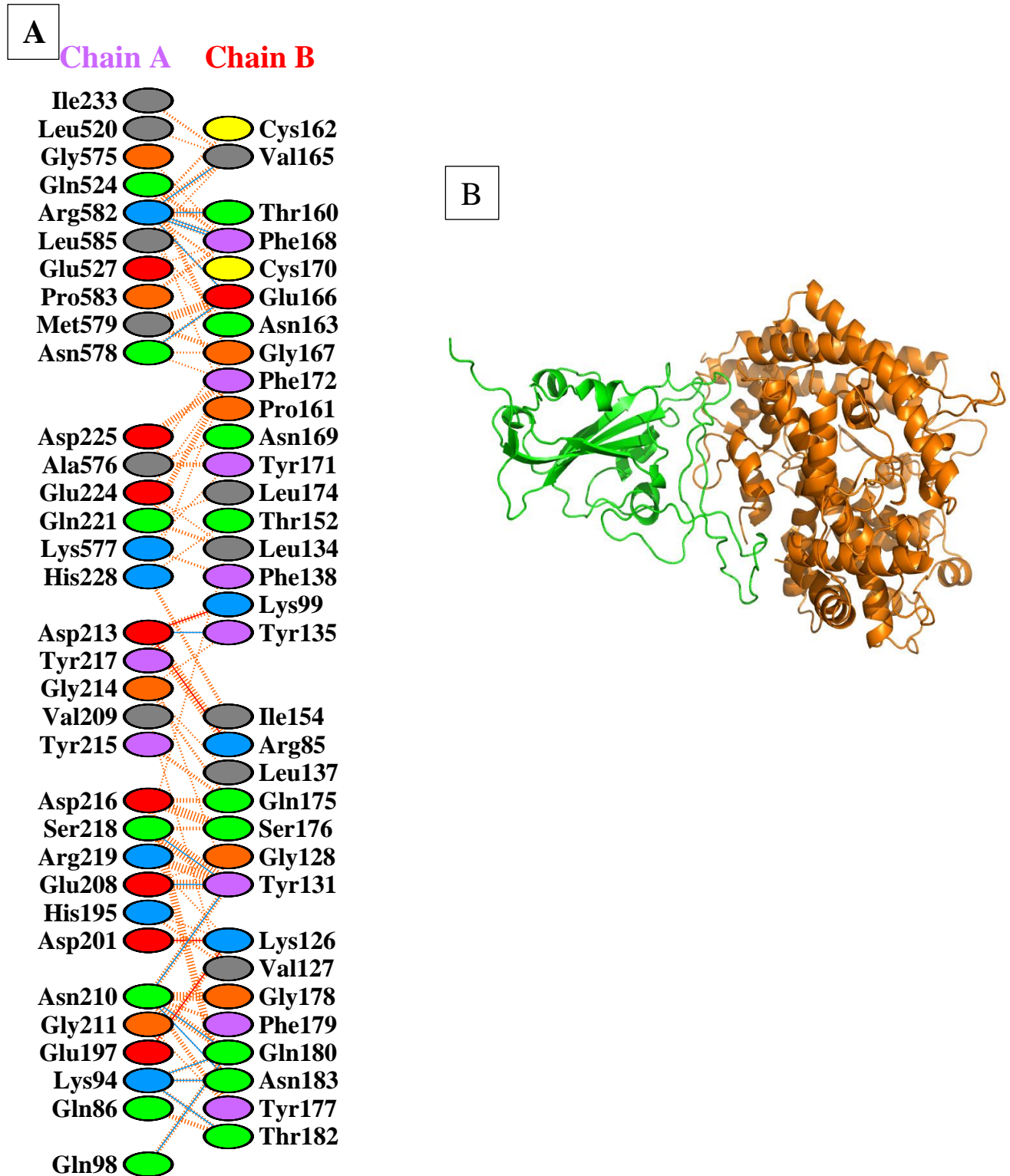




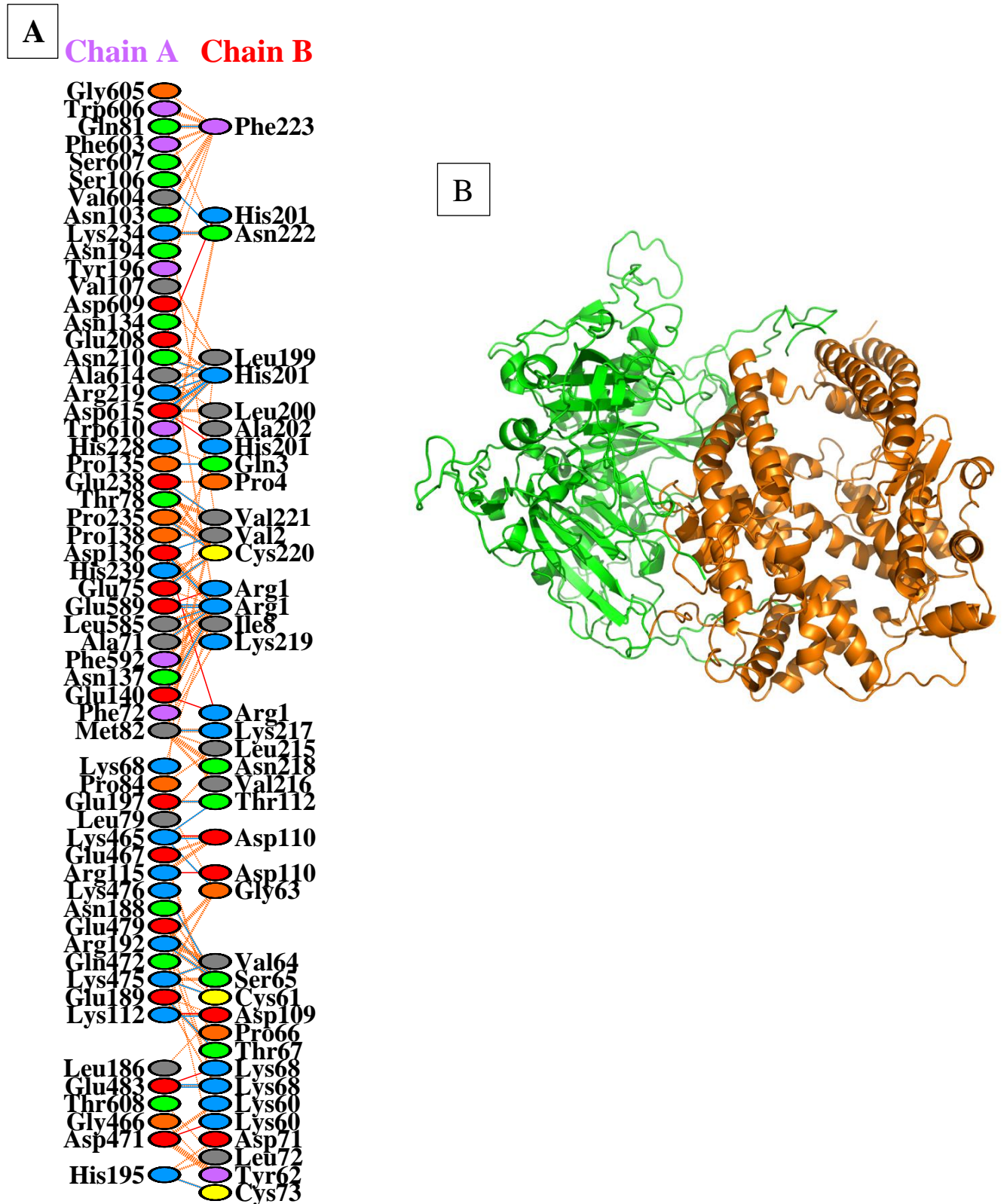
**Supplementary Figure 2F: Protein–protein docking representation of hACE2 and RBD of B.1.1.529 (Omicron) (EPI\_ISL\_6640917).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



**Supplementary Figure 2G: Protein–protein docking representation of hACE2 and RBD of C.37(Lambda) (EPI\_ISL\_1111334).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

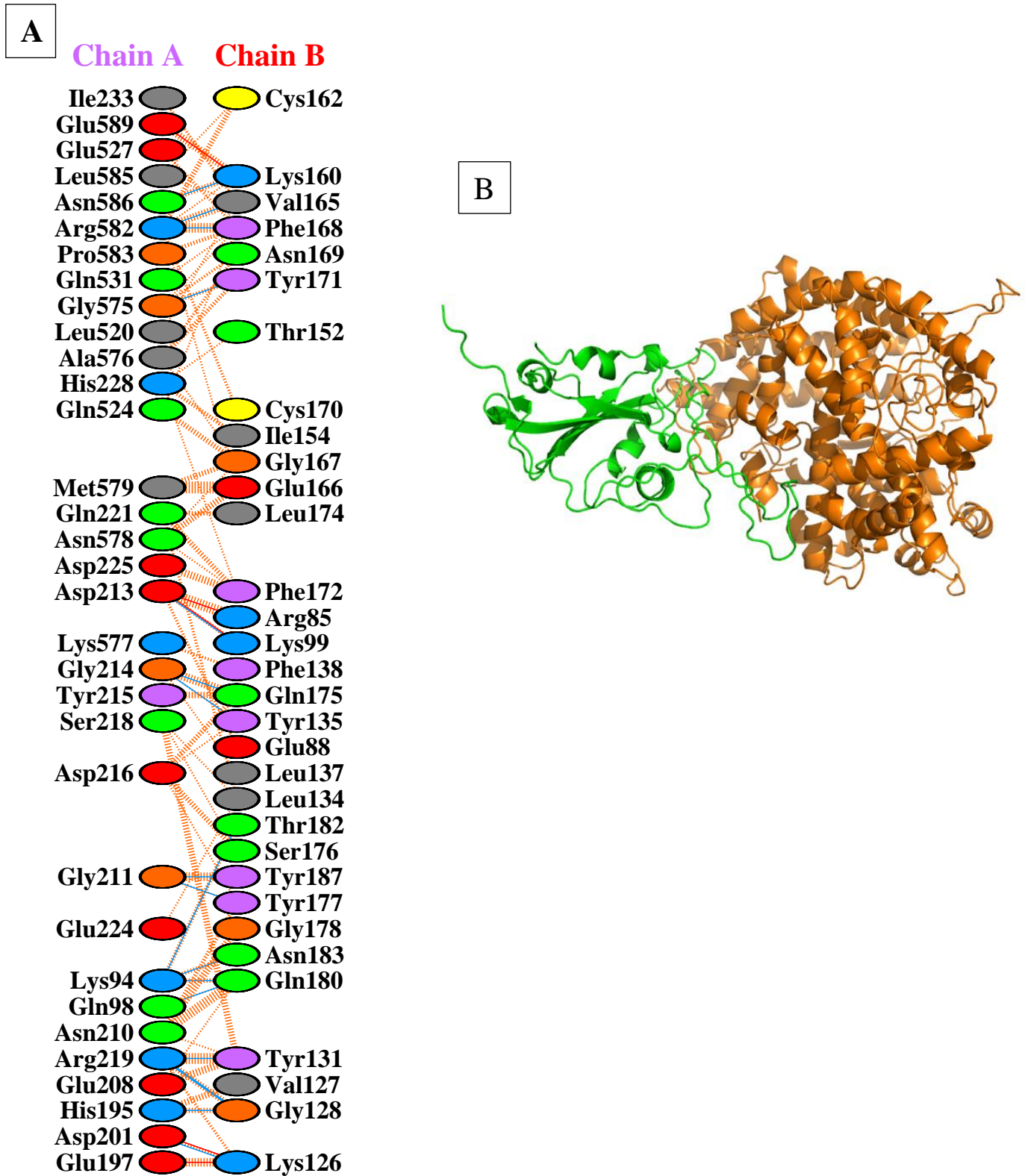


**Supplementary Figure 2H: Protein–protein docking representation of hACE2 and RBD of B.1.621(Mu) (EPI\_ISL\_3369952).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



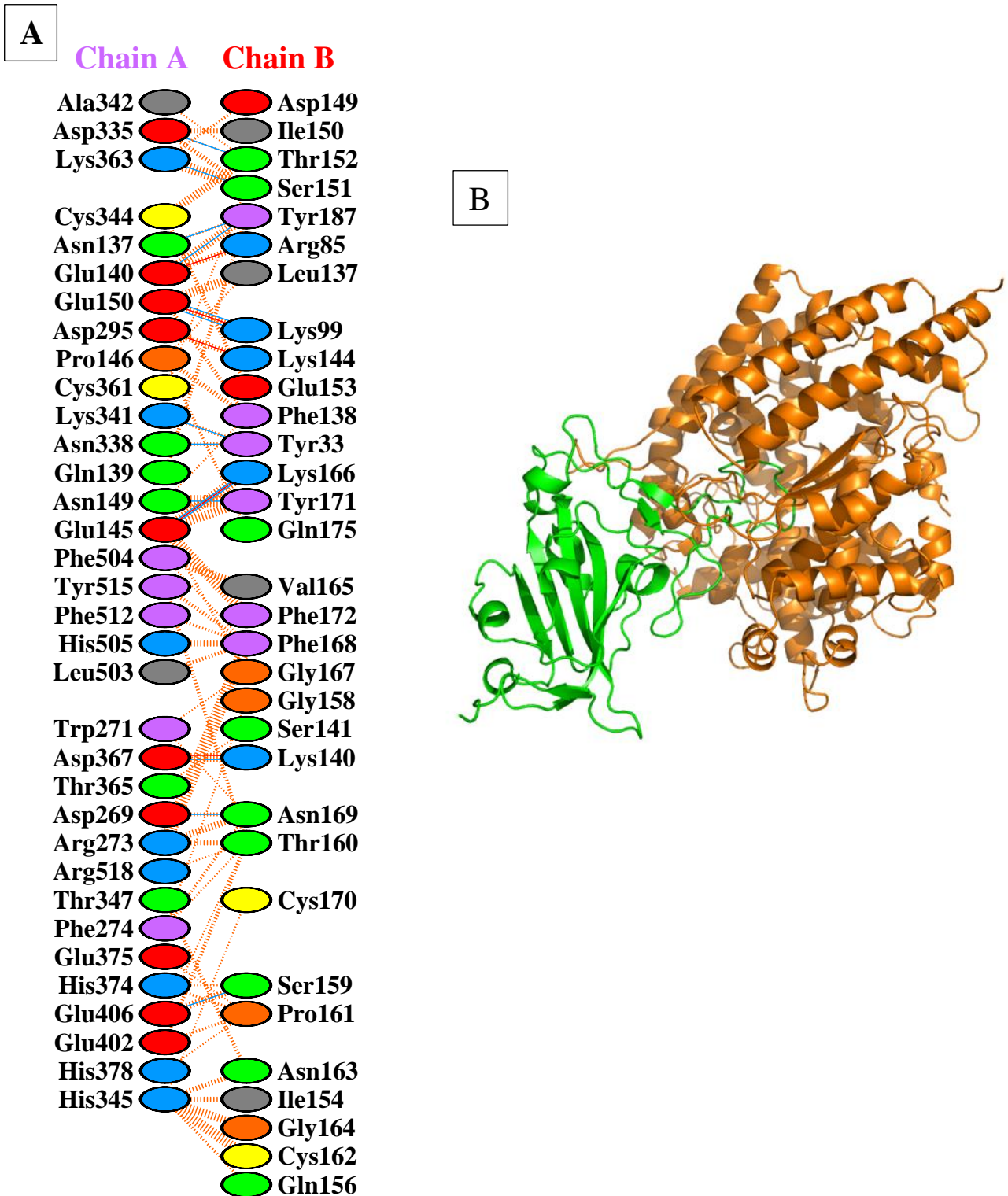
**Supplementary Figure 2I: Protein–protein docking representation of hACE2 and RBD of B.1.427/B.1.429 (Epsilon) (EPI\_ISL\_648527).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



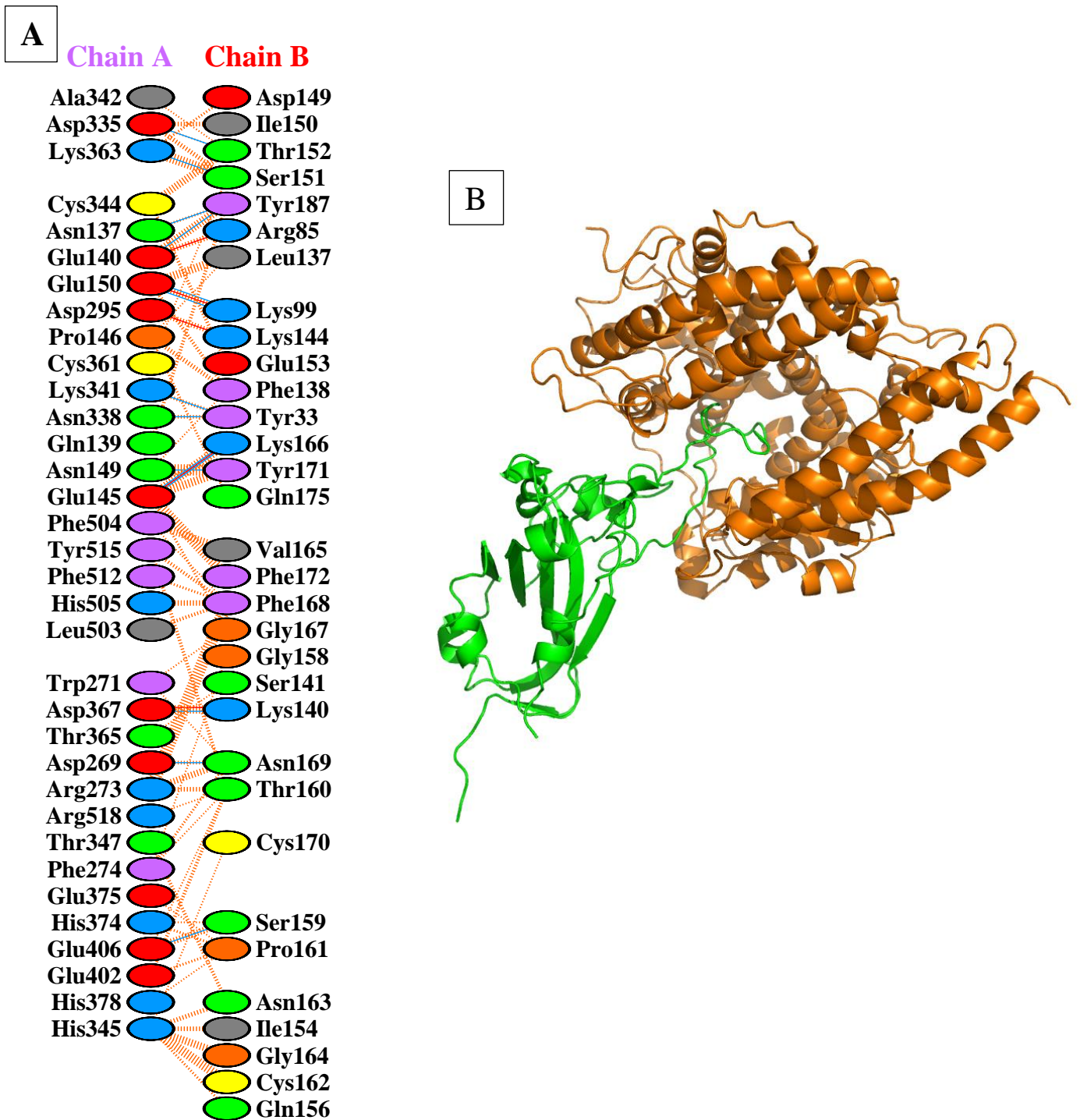


**Supplementary Figure 2J: Protein–protein docking representation of hACE2 and RBD of B.1.1.519 (EPI\_ISL\_721617).**

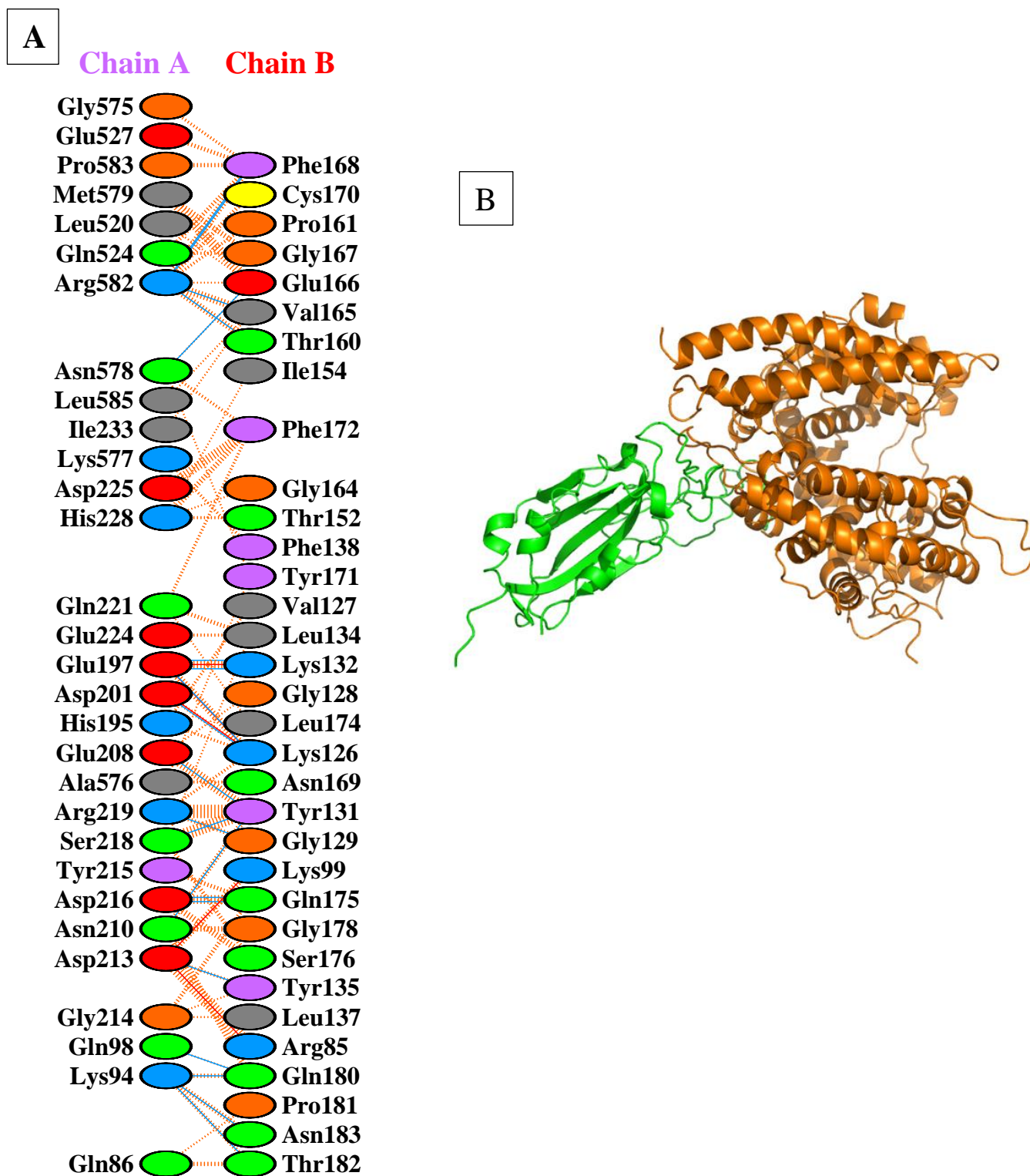
(A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



**Supplementary Figure 2K: Protein–protein docking representation of hACE2 and RBD of R.1 (EPI\_ISL\_736897).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

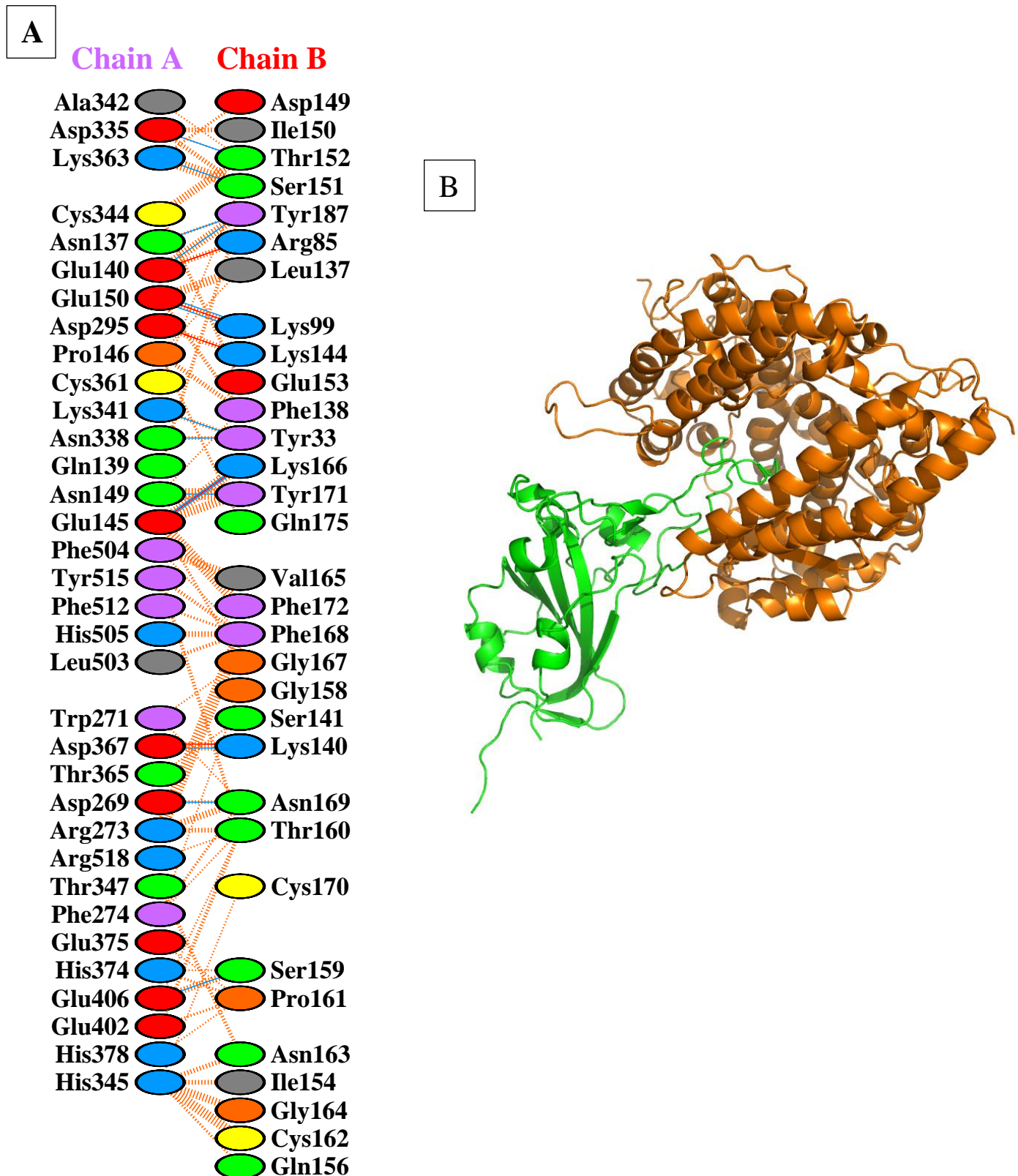


**Supplementary Figure 2L: Protein–protein docking representation of hACE2 and RBD of B.1.525(Eta) (EPI\_ISL\_760883).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

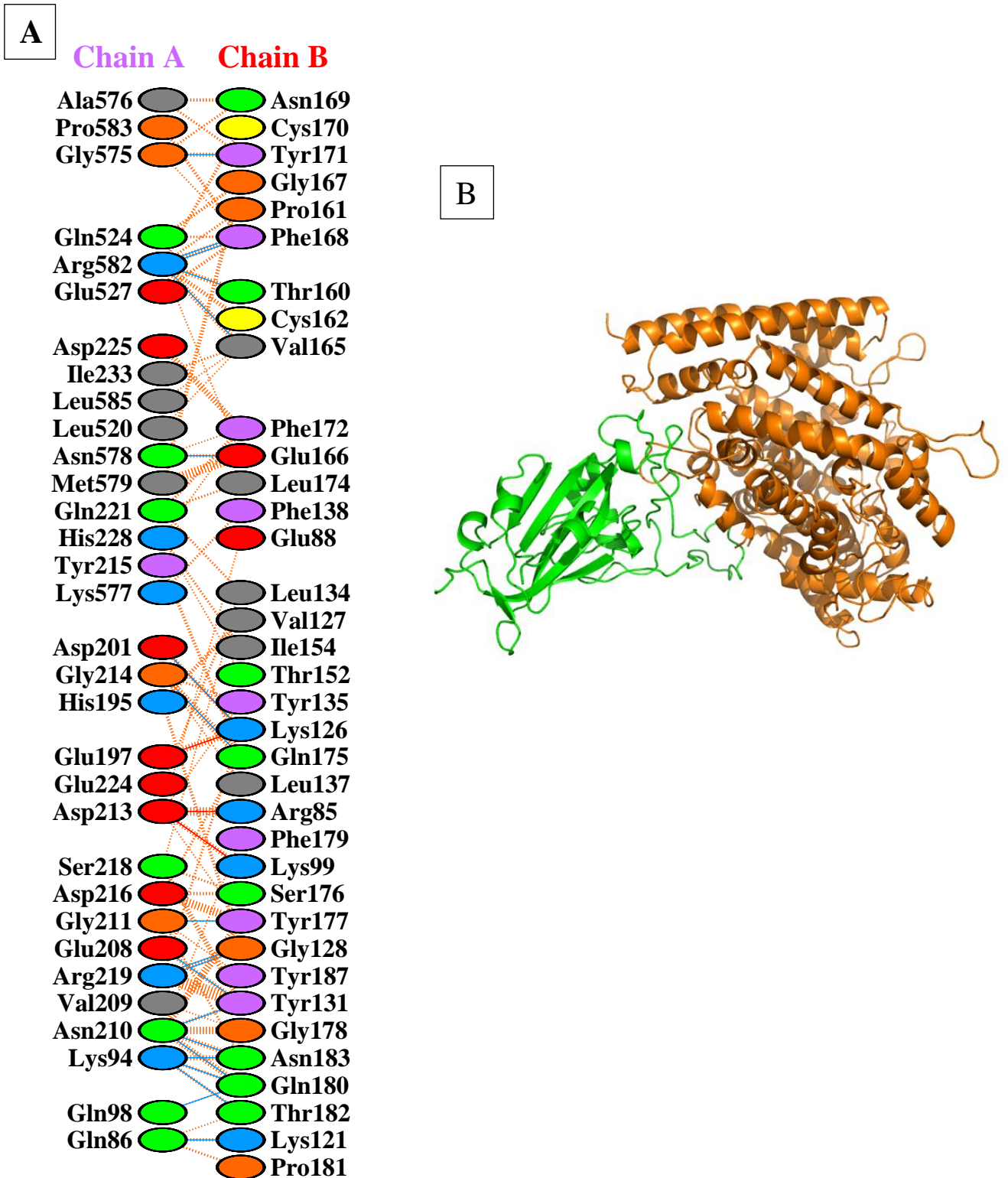


**Supplementary Figure 2M: Protein–protein docking representation of hACE2 and RBD of B.1.214.2 (EPI\_ISL\_760951).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

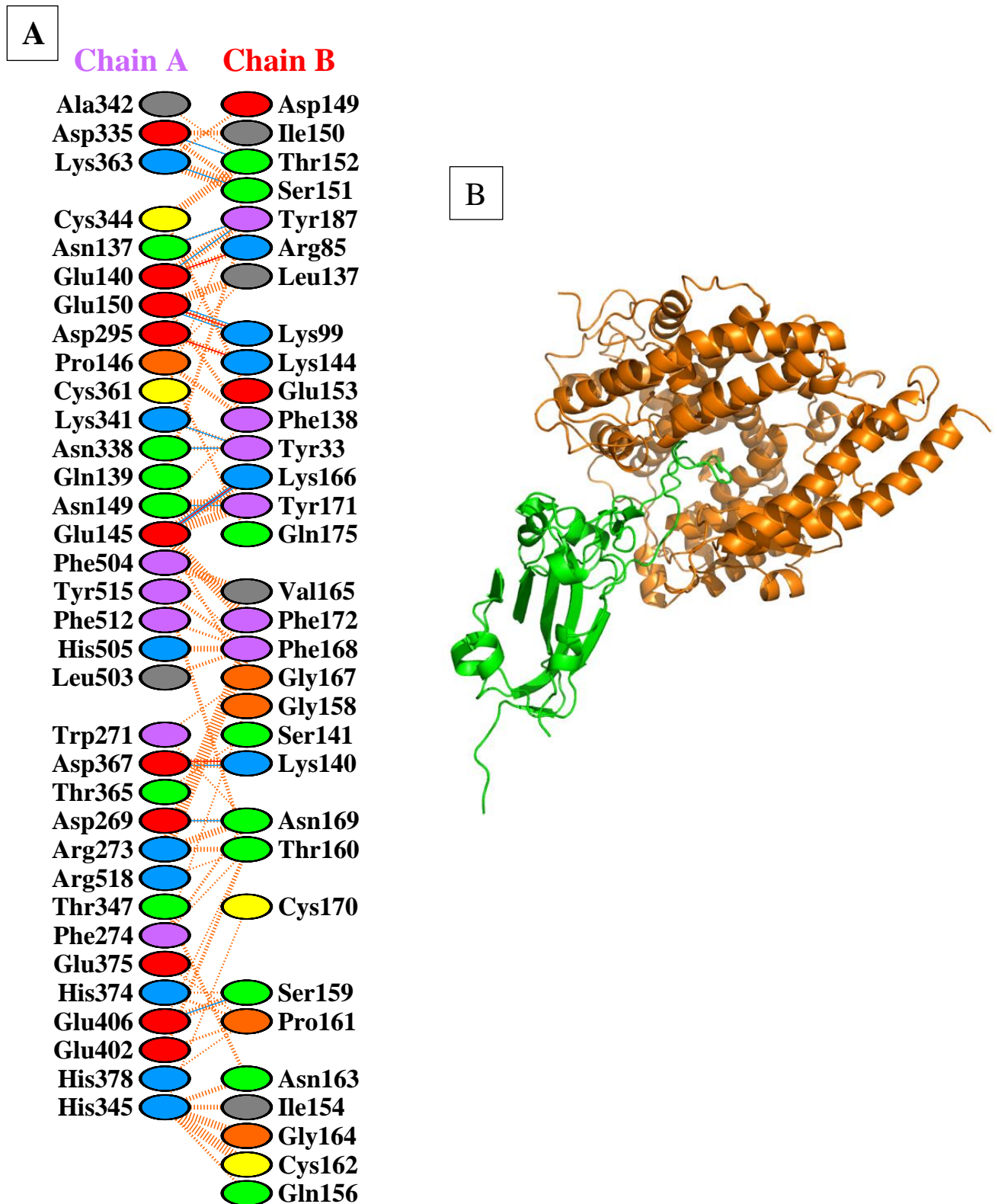




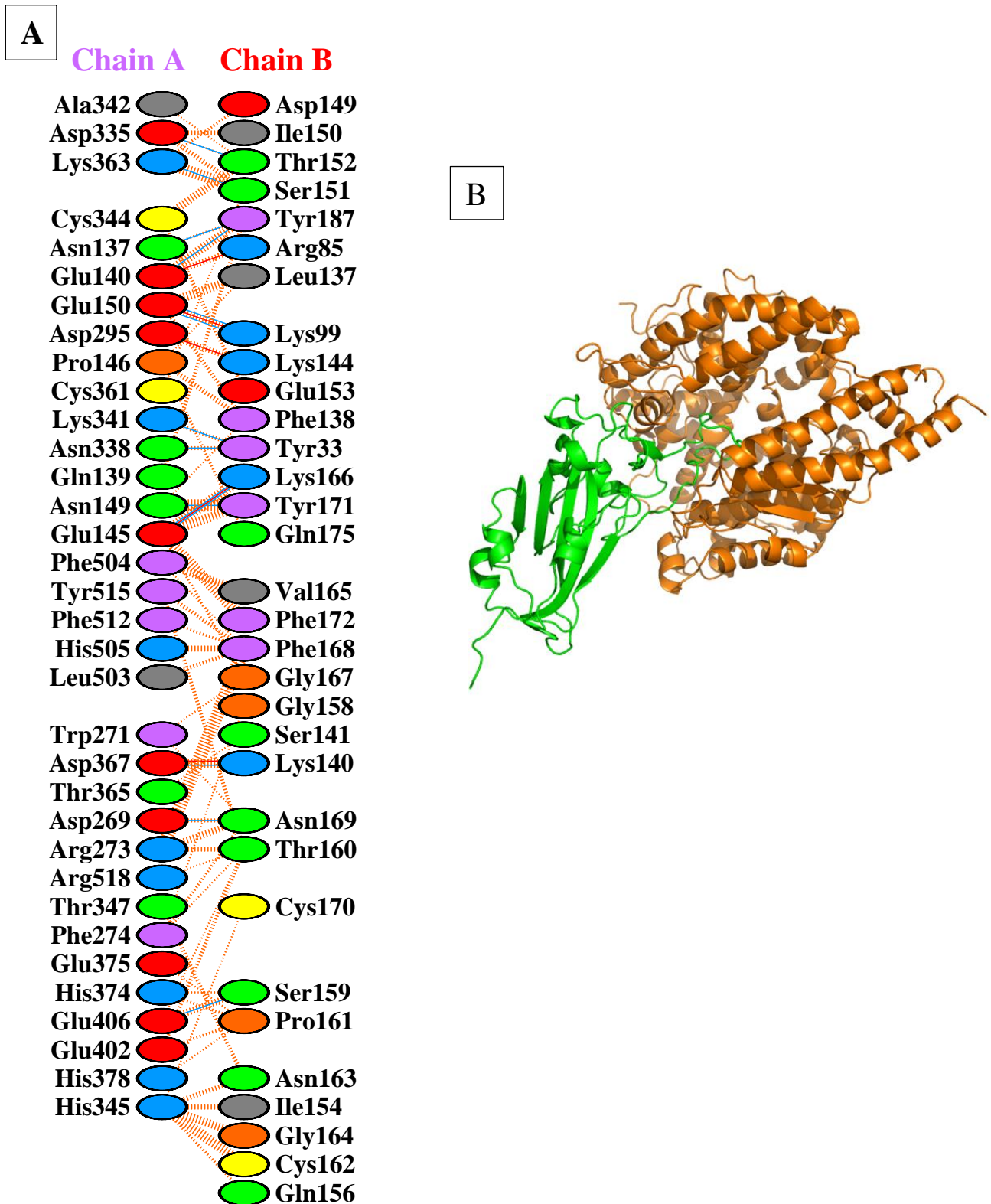
**Supplementary Figure 2N: Protein–protein docking representation of hACE2 and RBD of B.1.526(Lota) (EPI\_ISL\_765494).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



**Supplementary Figure 20: Protein–protein docking representation of hACE2 and RBD of B.1.466.2 (EPI\_ISL\_877419).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

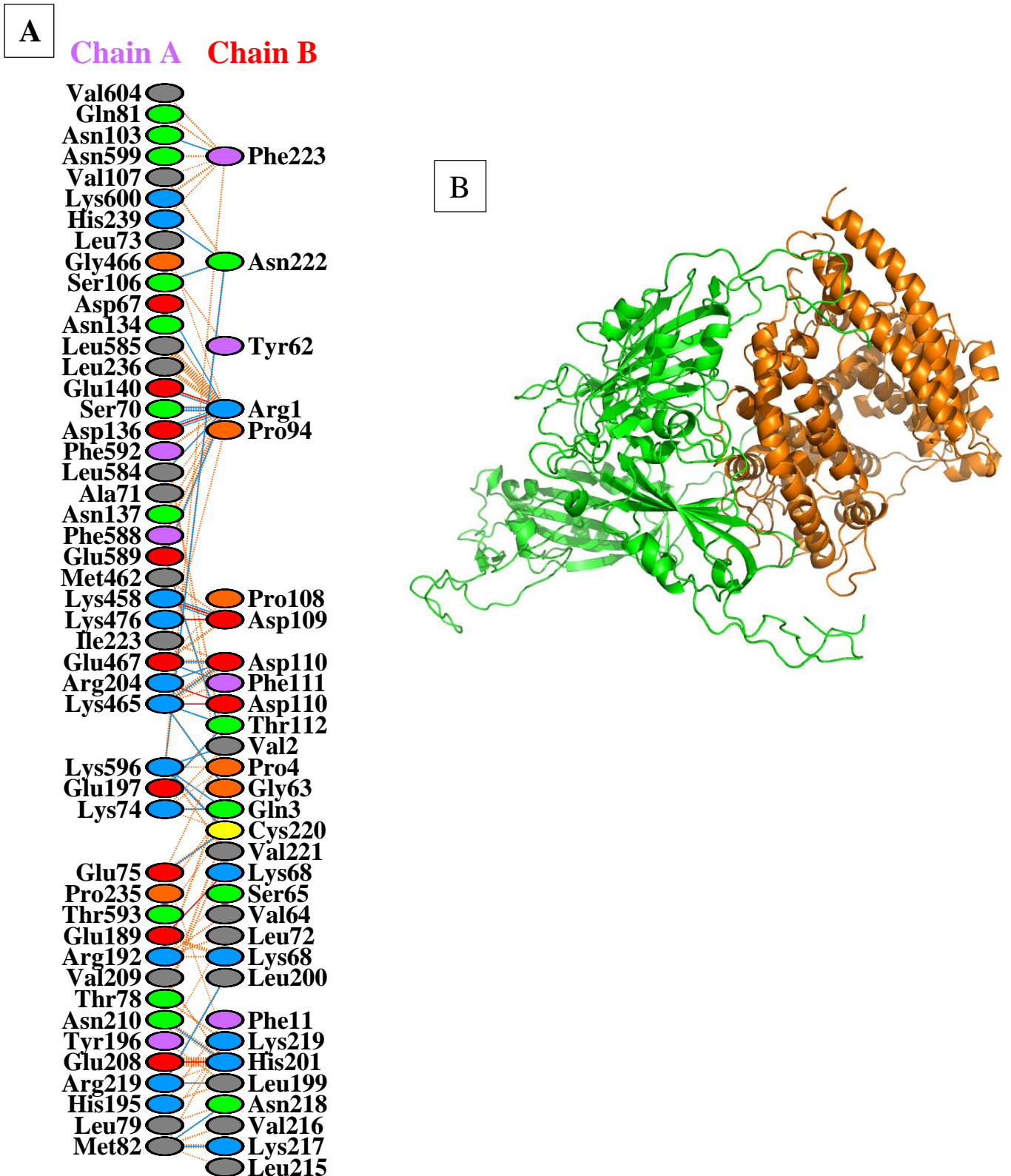


**Supplementary Figure 2P: Protein–protein docking representation of hACE2 and RBD of B.1.1.318 (EPI\_ISL\_937654).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

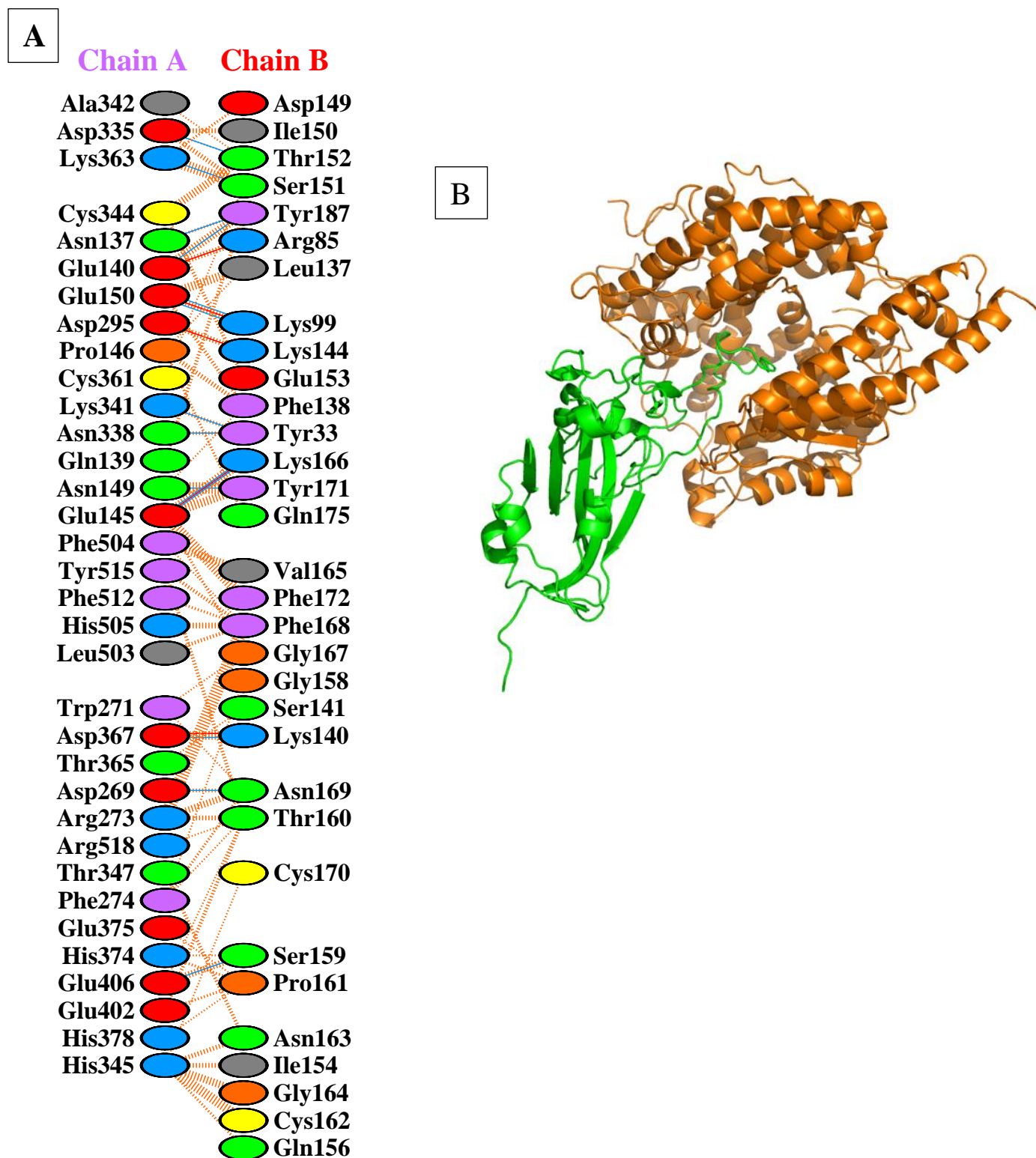


**Supplementary Figure 2Q: Protein–protein docking representation of hACE2 and RBD of B.1.619 (EPI\_ISL\_1150929).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

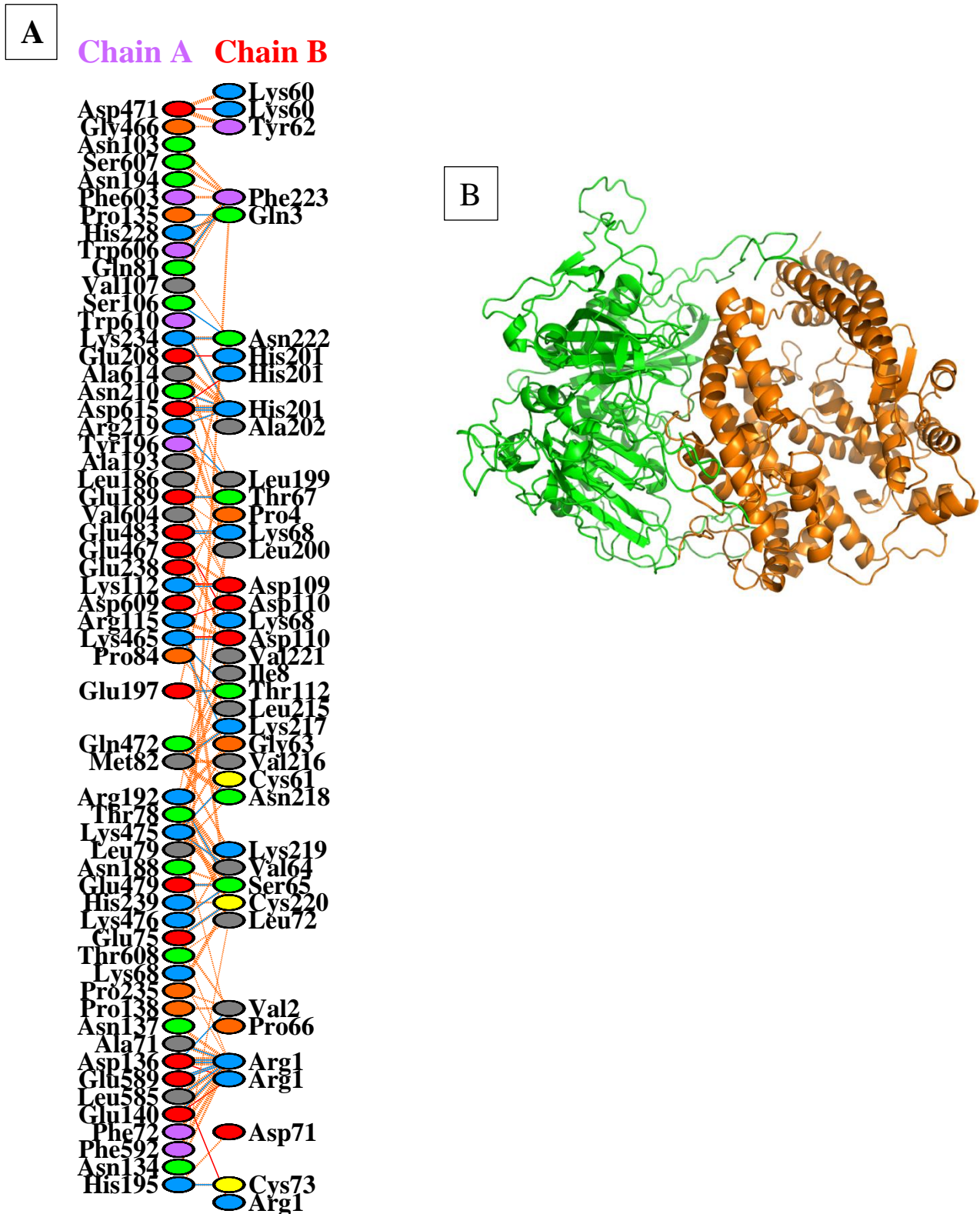




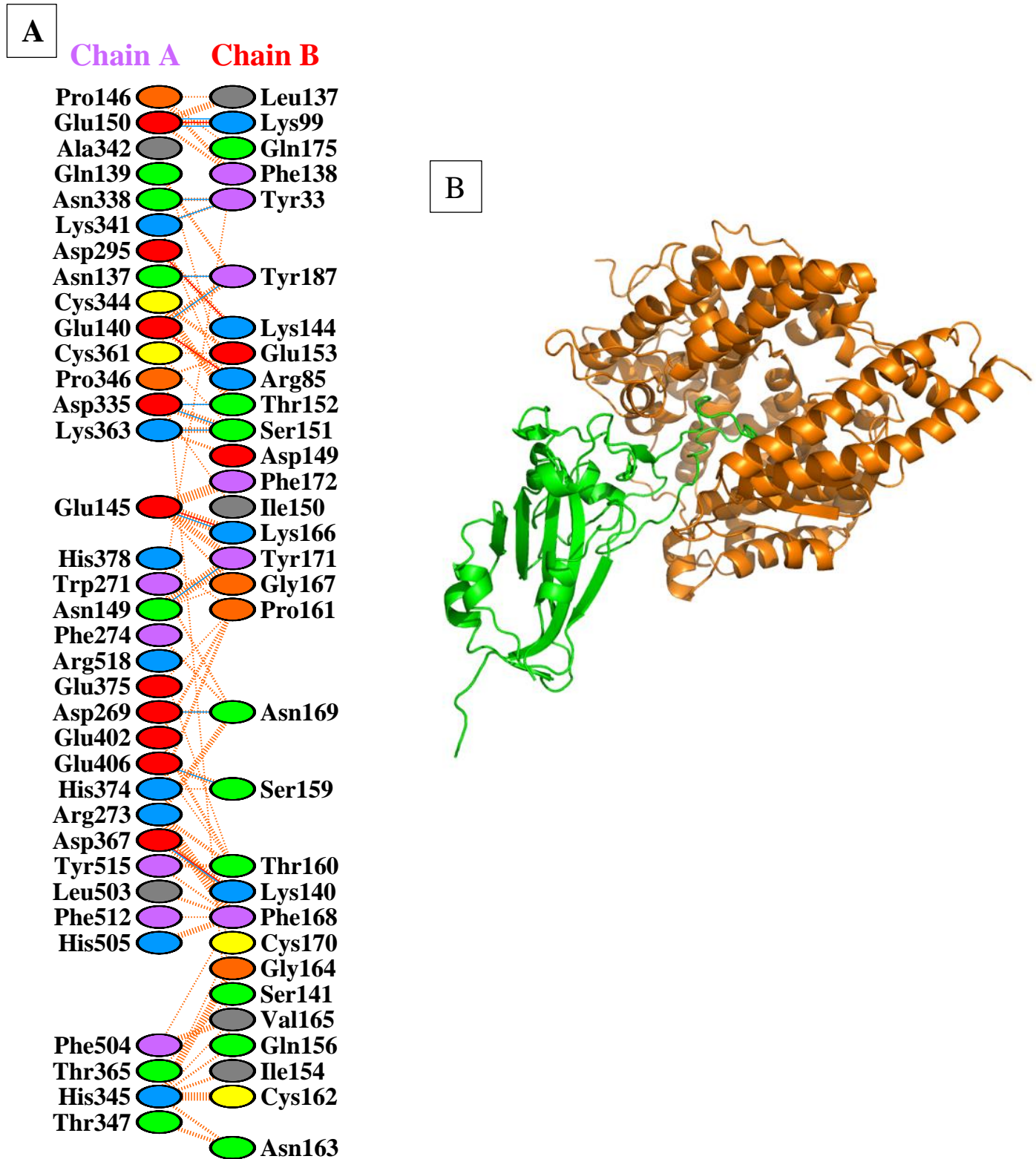
**Supplementary Figure 2R: Protein–protein docking representation of hACE2 and RBD of C.36.3 (EPI\_ISL\_1237137).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



**Supplementary Figure 2S: Protein–protein docking representation of hACE2 and RBD of AT.1 (EPI\_ISL\_1259283).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

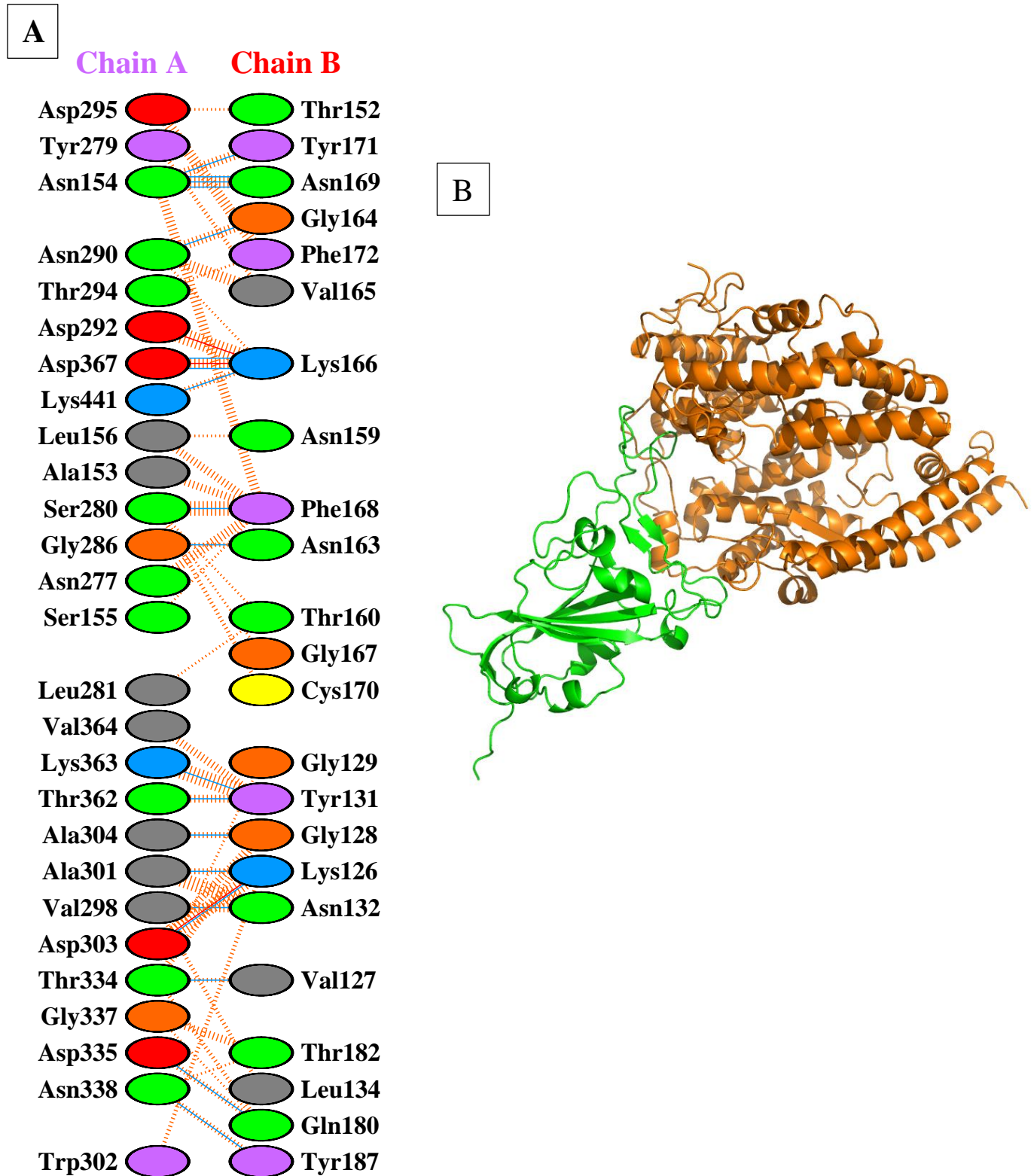


**Supplementary Figure 2T: Protein–protein docking representation of hACE2 and RBD of B.1.617.1(Kappa) (EPI\_ISL\_1357699).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

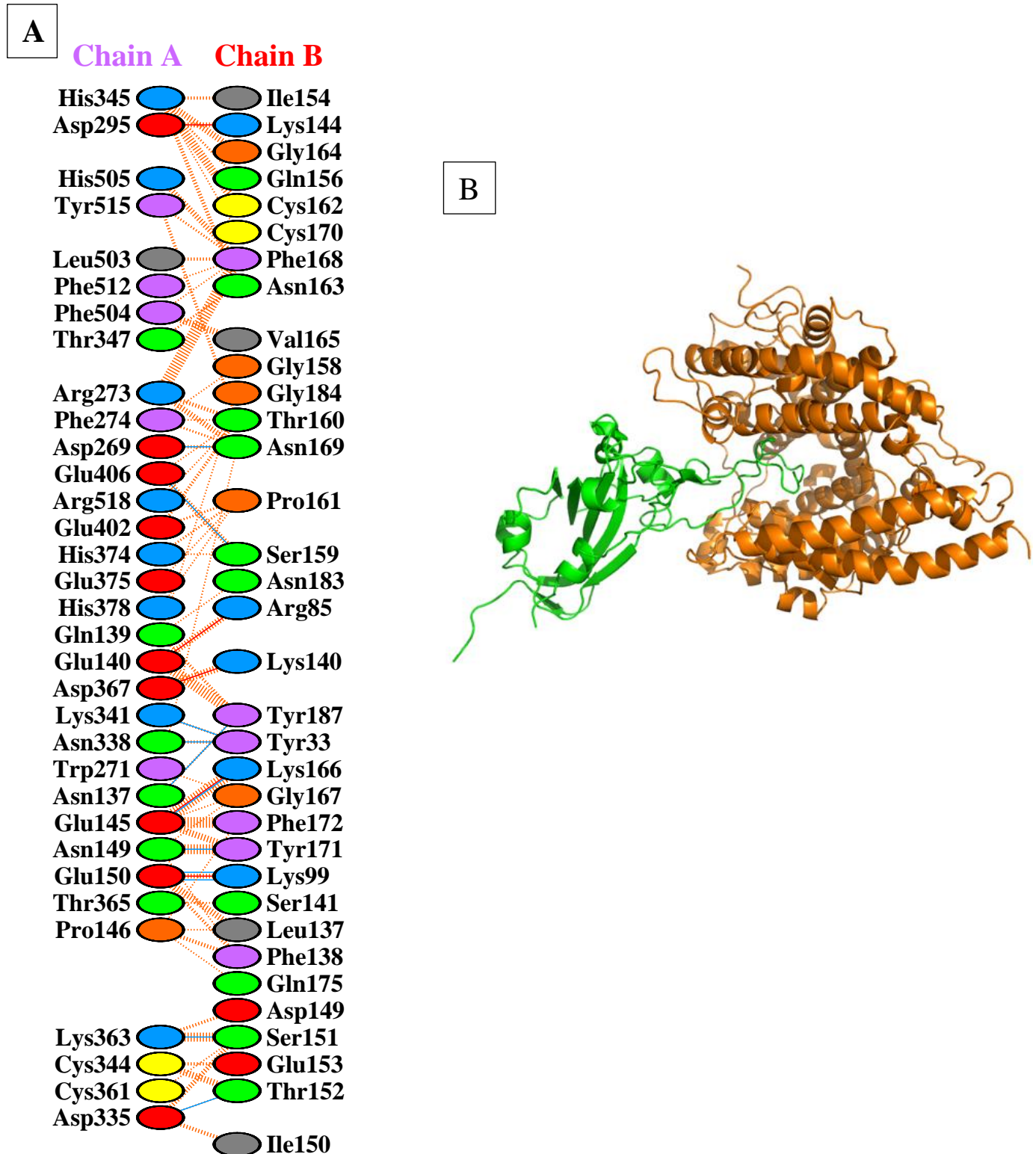


**Supplementary Figure 2U: Protein–protein docking representation of hACE2 and RBD of B.1.1.523 (EPI\_ISL\_1448584) .** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

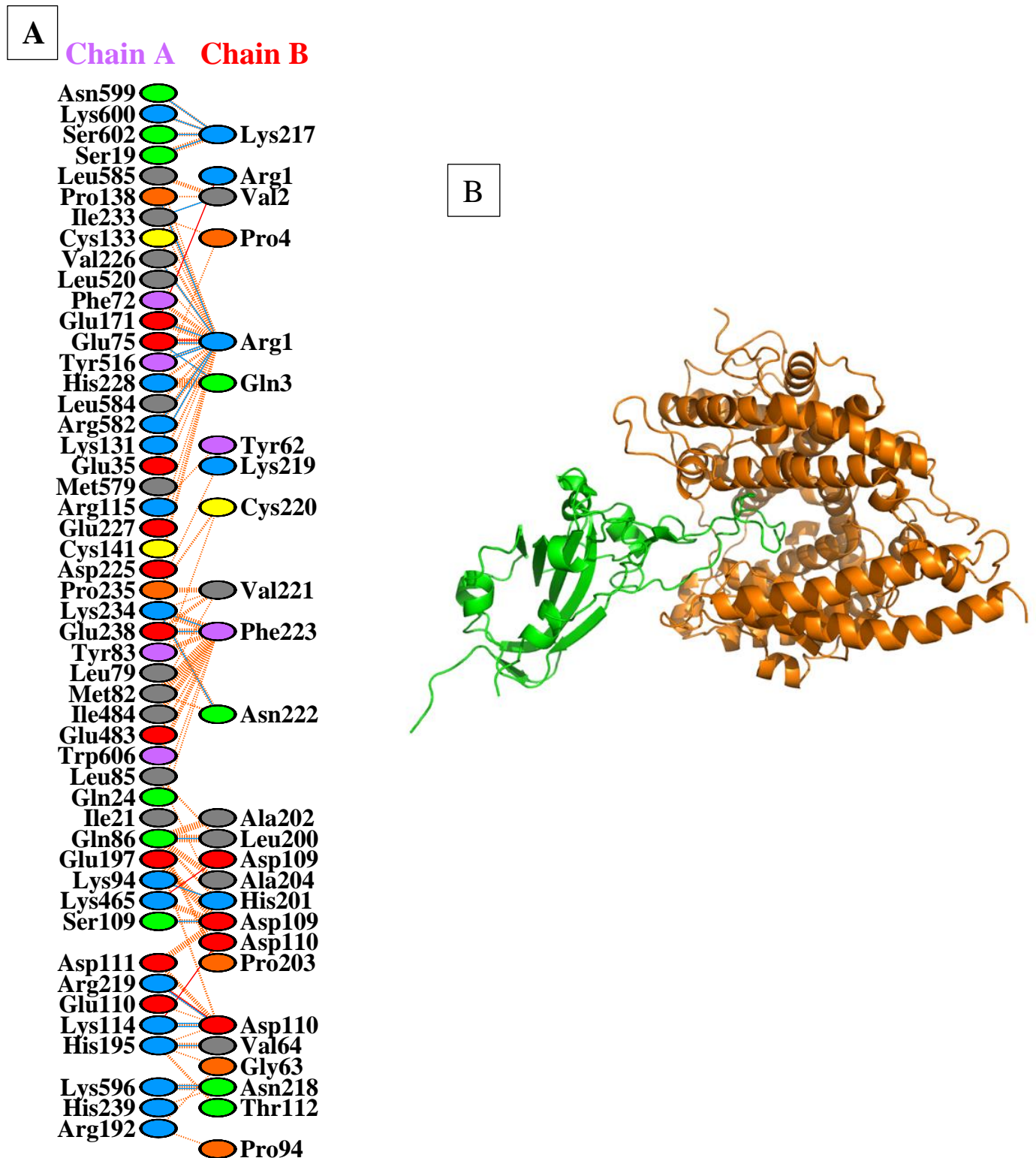




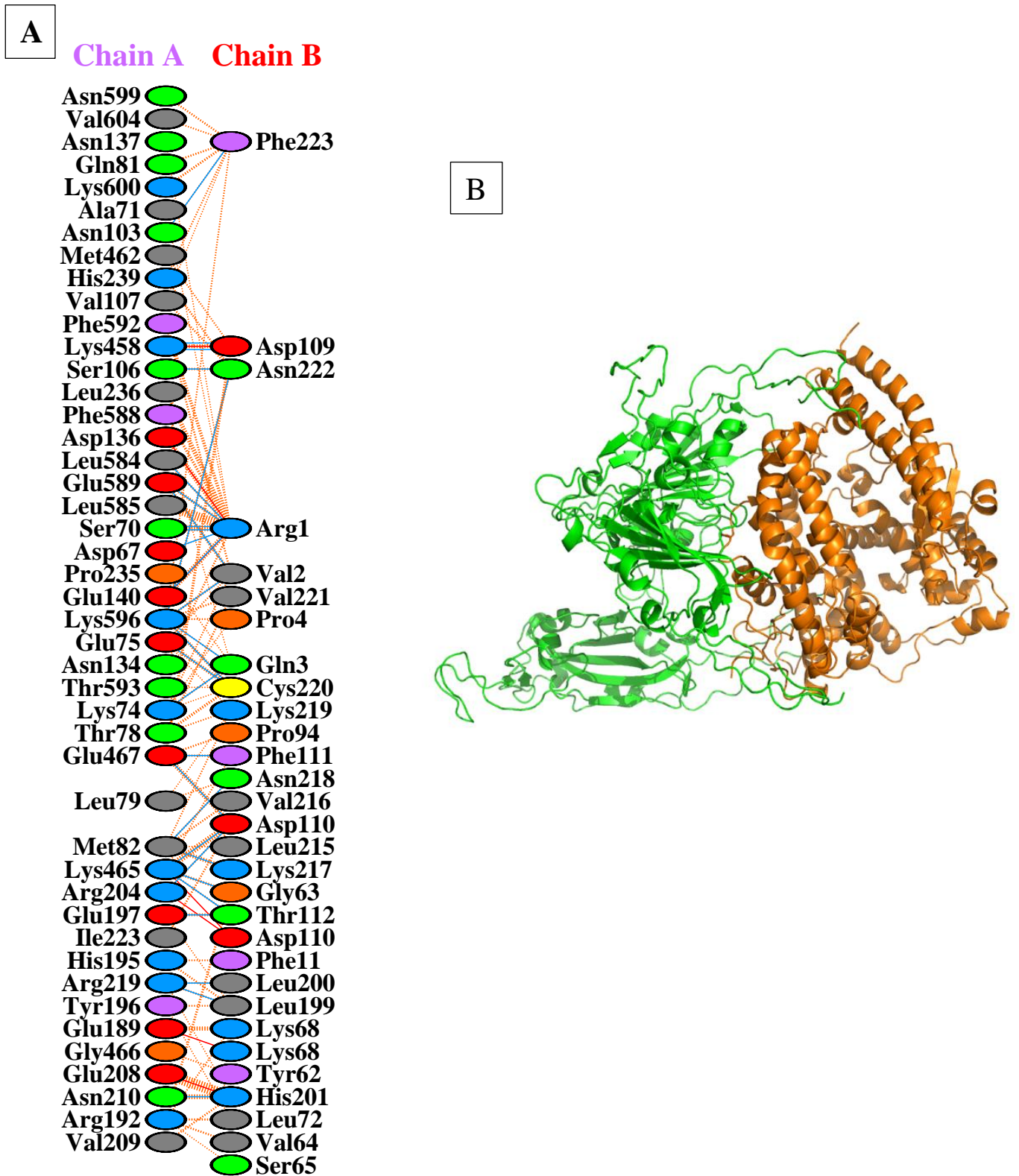
**Supplementary Figure 2V: Protein–protein docking representation of hACE2 and RBD of B.1.620 (EPI\_ISL\_1579527).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



**Supplementary Figure 2W: Protein–protein docking representation of hACE2 and RBD of AV.1 (EPI\_ISL\_1595332).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex

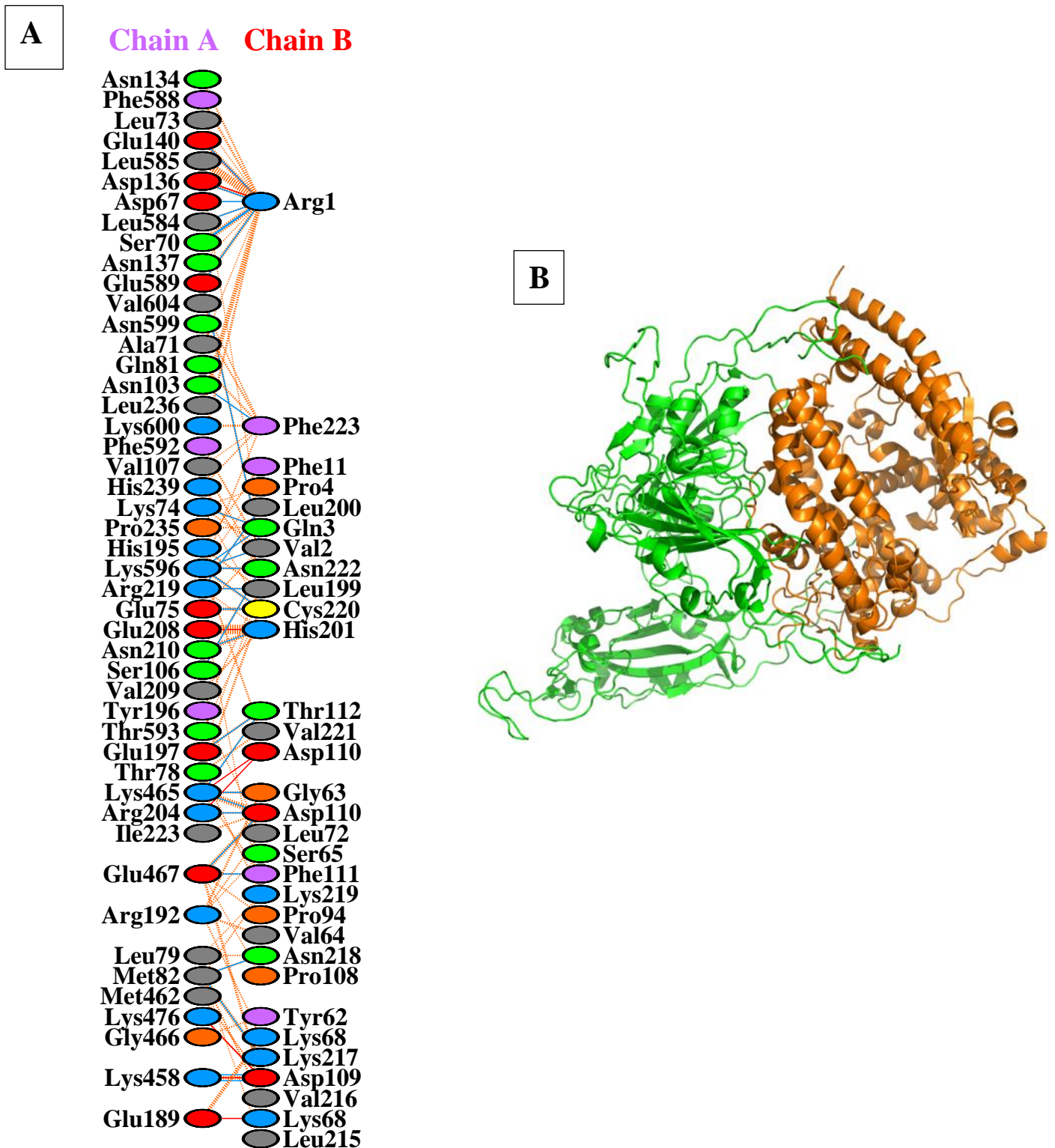


**Supplementary Figure 2X: Protein–protein docking representation of hACE2 and RBD of B.1.630 (EPI\_ISL\_3045385).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex



**Supplementary Figure 2Y: Protein–protein docking representation of hACE2 and RBD of C.1.2 (EPI\_ISL\_3447714) . (A)** The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. **(B)** The binding interface of hACE2:RBD complex





**Supplementary Figure 22: Protein–protein docking representation of hACE2 and RBD of B.1.640 (EPI\_ISL\_5592661).** (A) The interaction representation, which includes hydrogen (—), salt bridges (—), and non-bonded (|||||) interactions. Chain A represents hACE2 and chain B represents RBD. Residue colors: positive (blue): H,K,R; negative (red): D,E; neutral (green): S,T,N,Q; aliphatic (grey): A,V,L,I,M; aromatic (purple): F,Y,W; Pro & Gly (orange): P,G. (B) The binding interface of hACE2:RBD complex