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Supplemental information

A highly potent antibody effective against SARS-CoV-2 variants of concern

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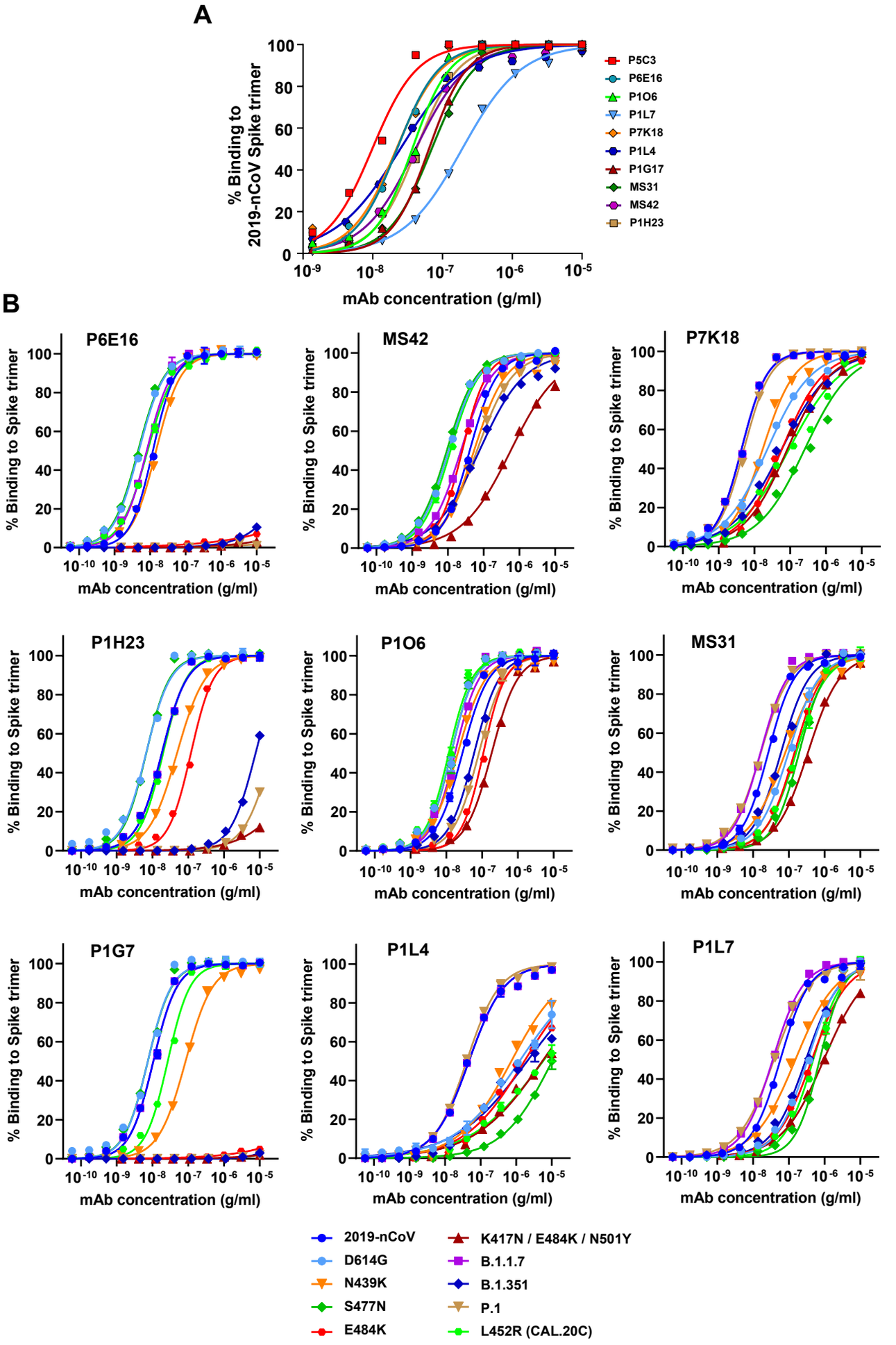

Figure S1: Binding affinity of anti-SARS-CoV-2 antibodies for 2019-CoV Spike and a panel of Spike proteins produced with variant residue identified in circulating SARS-CoV-2 viruses. Relates to Figure 1.

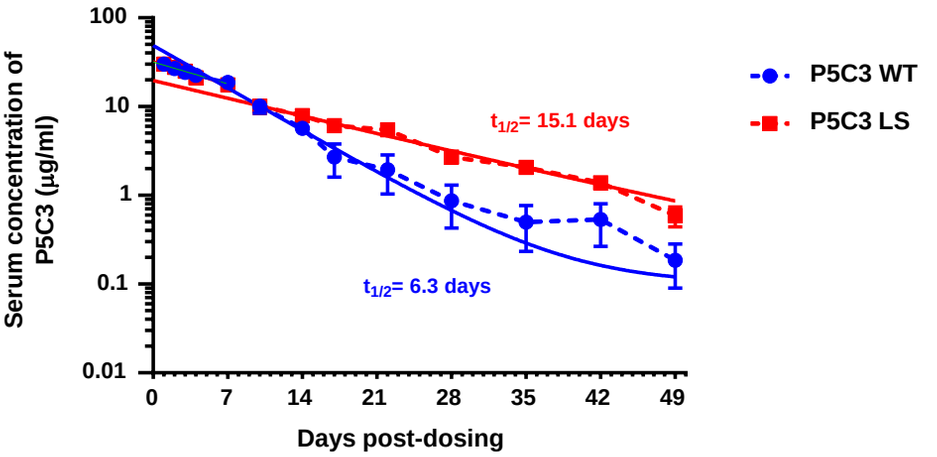

Figure S2: Pharmacokinetic properties of P5C3 and P5C3 LS in the human FcRn Tg32 transgenic mouse model. Relates to Figure 3.

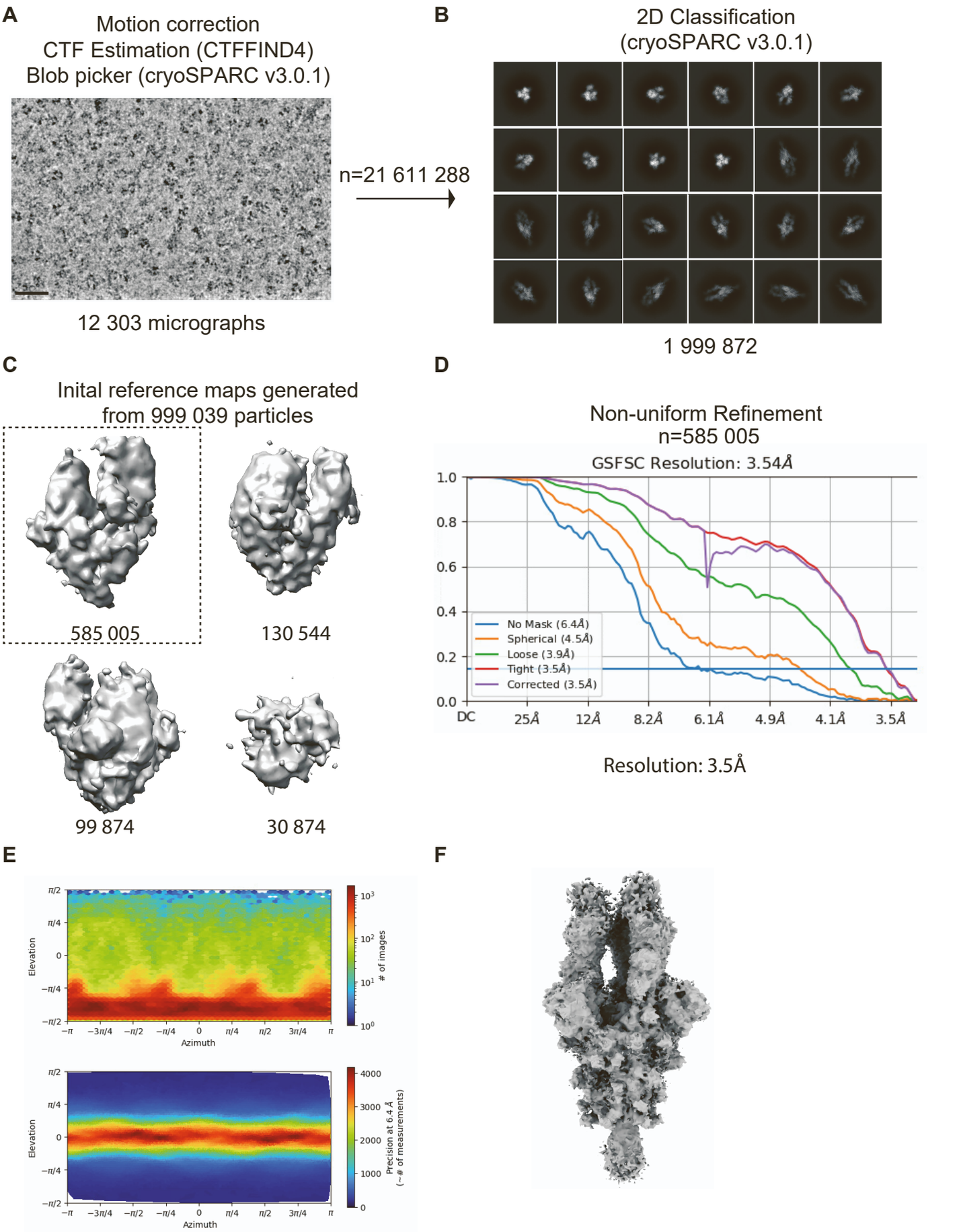

Figure S3: Cryo-EM structure determination of P5C3 Fab in complex with SARS-CoV-2 Spike. **(A)** A representative micrograph from the 12 303 micrographs. Scale bar is 50nm **(B)** Representative 2D class averages used for four ab Initio structure reconstruction. **(C)** 3D Class obtained after ab Initio reconstruction. Shown with a black rectangle is ab Initio 3D class used for no-uniform refinement **(D)** Fourier shell correlation (FSC) for the density maps obtained by non-uniform refinement with C1 symmetry. **(E)** Orientations of all particles used in the final refinement are shown as a heat map. **(F)** Unsharpened cryo-EM map for spike trimer with bound P5C3 Fab. Relates to Figure 4 and 5.

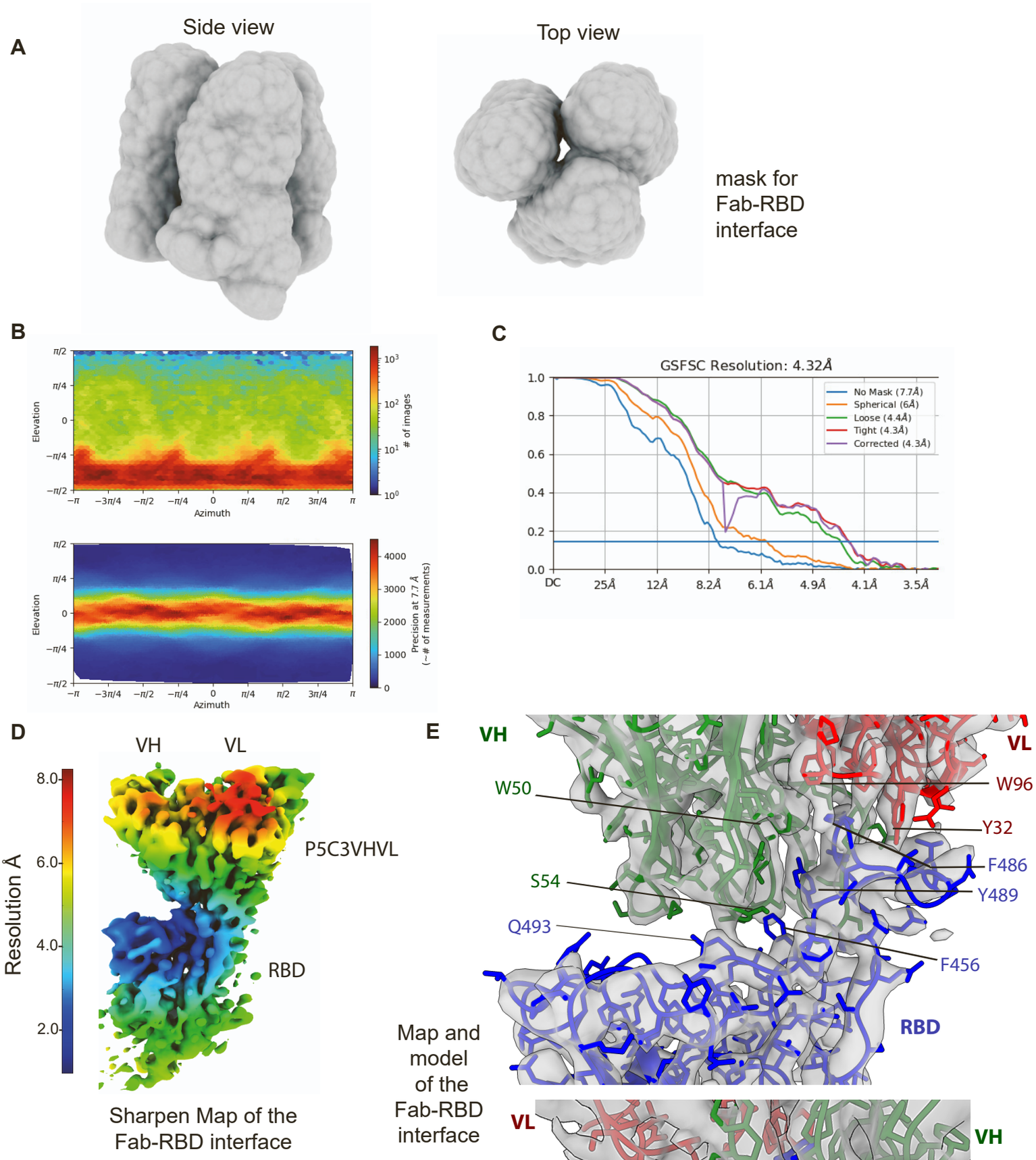

Figure S4: Cryo-EM structure refinement of P5C3 Fab-RBD interface. **(A)** Mask used for local refinement of the Fab-RBD interface side and top view. **(B)** Orientations of all particles used in the final refinement are shown as a heat map **(C)** Fourier shell correlation (FSC) for the density maps obtained by non-uniform refinement with C1 symmetry. **(D)** Sharpened map of the local refinement. **(E)** PDB model placed in the sharpened local refinement map with select residues from the RBD, VH and VL shown in blue, green and red text, respectively. Relates to Figure 4 and 5.

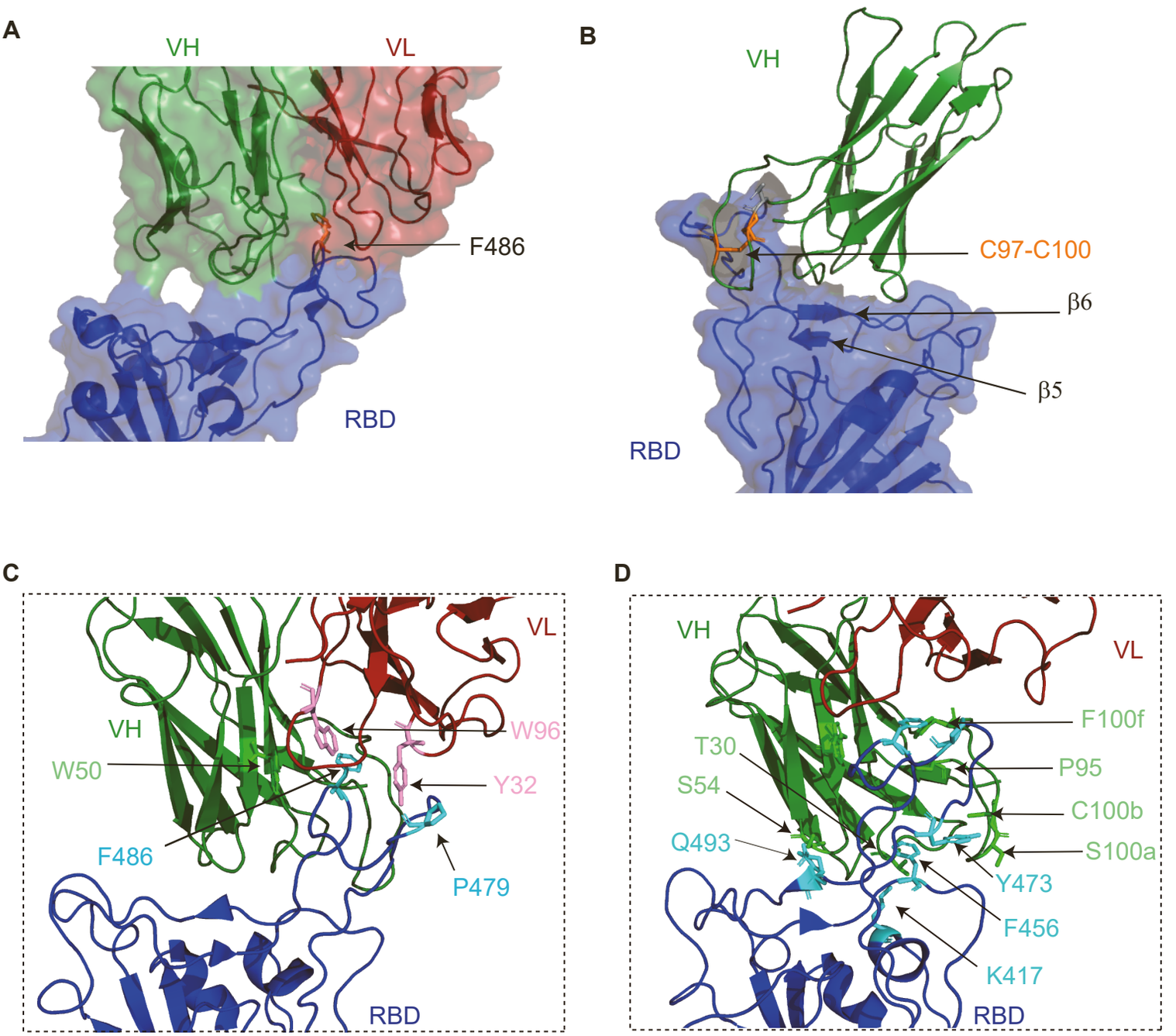

Figure S5: Structural details of P5C3 Fab interaction with the SARS-CoV-2 RBD. **(A)** P5C3 Fab is centered on the phenylalanine in position 486 of the RBD. Shown as licorice. **(B)** Disulfide bridges between C97 and C100b is shown in orange. **(C-D)** Cartoon representation of the main P5C3 Fab light chain and heavy chain interaction with RBD. Select residues involved in the interaction are shown in cyan for RBD and pink for the P5C3 light chain and green for the P5C3 heavy chain. **(E)** RBD surface bound by P5C3 (orange), ACE2 (green) and shared by both (grey). Relates to Figure 4 and 5.

Table S1. Amino acid substitutions and deletions on SARS-CoV-2 variants of concern. Relates to Figure 5.

SARS-CoV-2 Variant	Spike mutations (RBD domain residues in bold)
Alpha / B.1.1.7 / 501Y.V1 (UK)	Δ69-70, Δ144, **N501Y**, A570D, D614G, P681H, T716I, S982A, D1118H
Beta / B.1.351 / 501Y.V2 (South African)	L18F, D80A, D215G, Δ242-244, R246I, **K417N, E484K, N501Y**, D614G, A701V
Gamma / P.1 / 501Y.V3 (Brazilian)	L18F, T20N, P26S, D138Y, R190S, **K417T, E484K, N501Y**, D614G, H655Y, T1027I, V1176F
Mink variant 16	L5F, Δ69-70, **Y453F**, D614G, N751Y, C1250F**)**
Cal.20C (Californian)	S13I, W152C, **L452R**
B.1.526 / B.1.232 (New York)	L5F, T95I, D253G, **E484K**, D614G, A701V

Table S2. Statistics of the Cryo-EM dataset and structure models EM data collection. Relates to Figure 4 and 5

Structure	Spike D614G+Fab P5C3	Local resolution Spike D614G+Fab P5C3
EMBD ID	EMD-13190	EMD-
PDB ID	7P40	
Data collection		
Microscope	Titan Krios	
Detector	Gatan Quantum-LS Energy Filter (GIF) with a Gatan K2 Summit direct electron detector.	
Voltage (KV)	300	300
Nominal magnification	105 000	105 000
Defocus range (μm)	0.8-2.5	0.8-2.5
Physical pixel (Å)	0.82	0.82
Electron dose (e^-/Å^2)	38	38
number of raw frames	30	30
Data processing		
Extracted particles (n)	21 611 288	
Refined particles (n)	1 999 872	
Particles for final map (n)	585 005	585 005
Symmetry imposed	C1	C1
Resolution	3.5	4.3
FSC threshold	0.143	0.143
Refinement		
Initial model used	PDB ID: 7K4N	
Map sharpening B-Factor (Å^2)	95.9	
composition (n)	9 Chains	3 Chains
Atoms	26466 (hydrogens: 0)	3309 (hydrogens: 0)
Residues	Protein: 3687	Protein:427
Ligands	0	0
Overall B-Factor (Å^2)	82.4	0.010 (0)
Protein (min/max/mean)	(-36.40/65.15/1.00)	(-49.3./184.66/3.79)
Ligand (min/max/mean)	0	0
Bonds (RMSD)		
length (Å) (n>4σ)	0.010 (0)	0.003 (0)
Angles (º) (n>4σ)	1.187 (1)	0.791 (1)
CC mask	0.72	0.73
Validation		
Ramachandran plot		
Residues favored (%)	91.32	87.89
Residues allowed (%)	7.86	11.88
Rotamer outliers (%)	0.83	0.28
Clash Score	8.06	15.92
MolProbity score	2.34	2.31