

Supplementary Information

Targeting ACE2 with a camelid antibody inhibits SARS-CoV-2 binding and has protective effects *in vivo*

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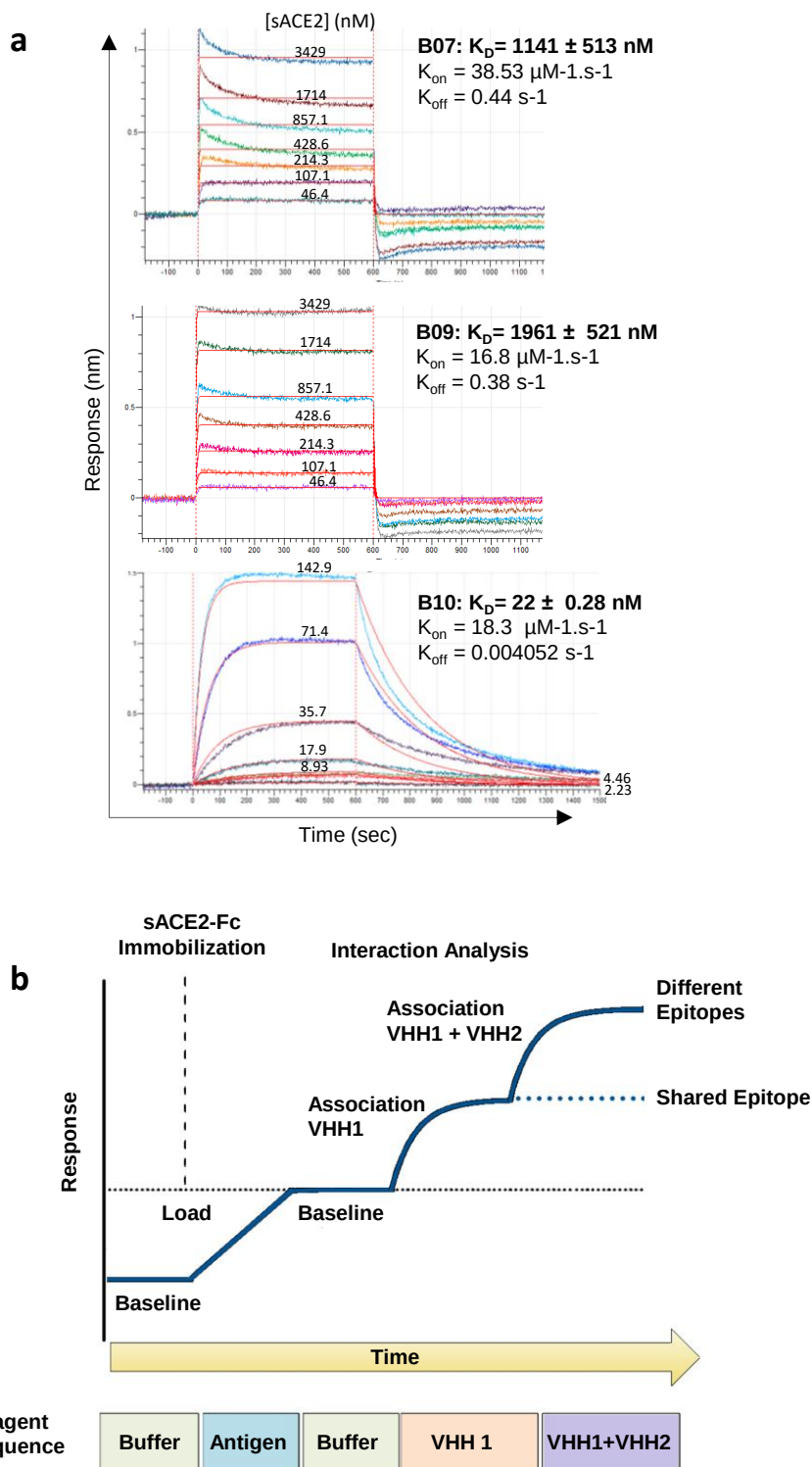
Supplementary Figures

Figures

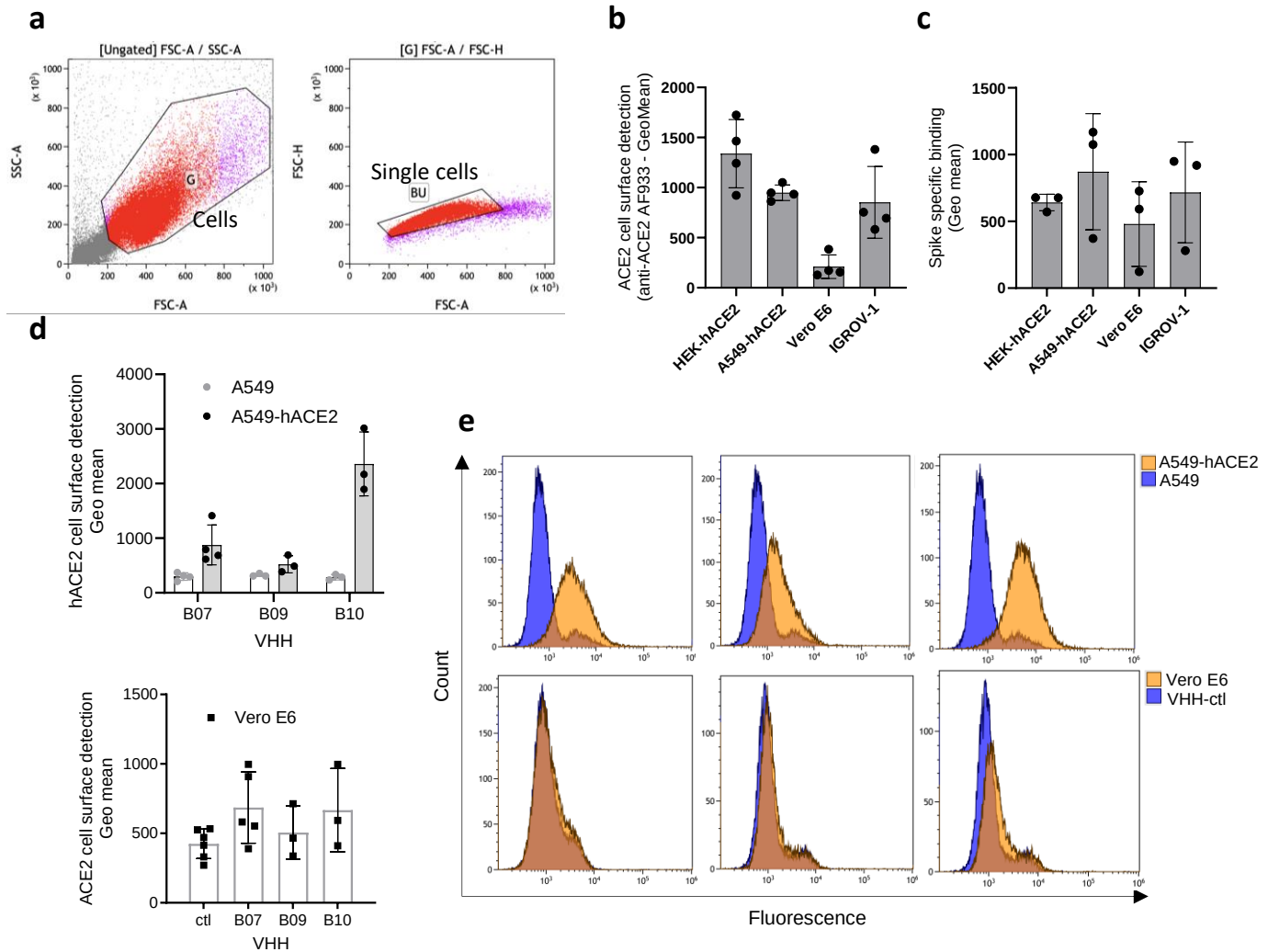
1. Sequence alignment of B07, B09, and B10 VHHs.
2. VHH binding on sACE2 and schematic of the binding competition assay.
3. VHHs binding on cells expressing ACE2.
4. Interactions between hACE2 and VHH B10.
5. Experimental 2|Fo|-|Fc| electron density maps at the site of interactions between hACE2 and VHHs.
6. Sequence alignment of human, hamster, and mouse ACE2.
7. Interactions of hACE2 with SARS-CoV-2 RBD (PDB: 6M0J) and footprints of interactions in different complexes.
8. Impact of hACE2 substitution on VHH binding.
9. B07-Fc activities.
10. Relative cell surface expression of ACE2 mutants and impact of substitutions on B07-Fc binding.
11. Separate color (top) or black and white (bottom) images of Fig. 7d.
12. Effect of VHH B07-Fc on hamsters.

Tables

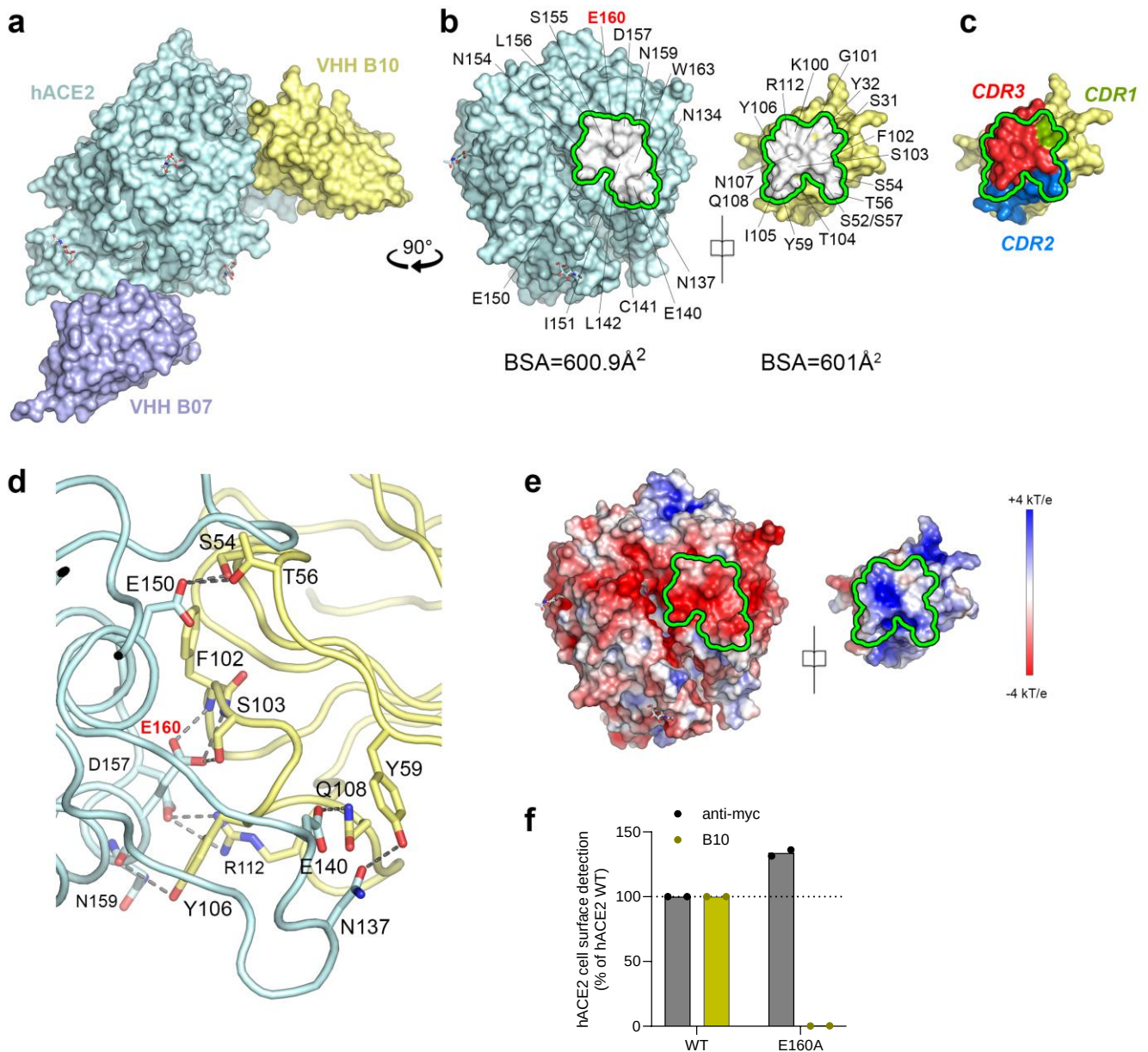
1. Statistical analyses and IC50 related to Fig. 4a and 6g (S-Fuse assay), and 6h (N detection).
2. Crystallization conditions, data collection, and refinement statistics.
3. Van der Waals and polar interactions between hACE2 and VHH B10.
4. Van der Waals and polar interactions between hACE2 and VHH B07.
5. Van der Waals contacts between hACE2 and VHH B07 and between hACE2 and RBDs for a selection of viruses using hACE2 as a receptor.



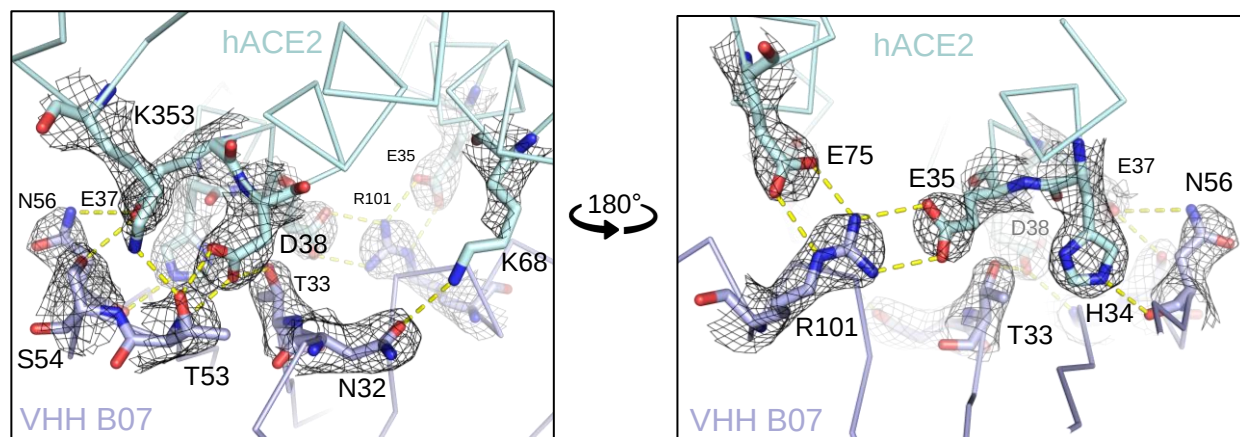
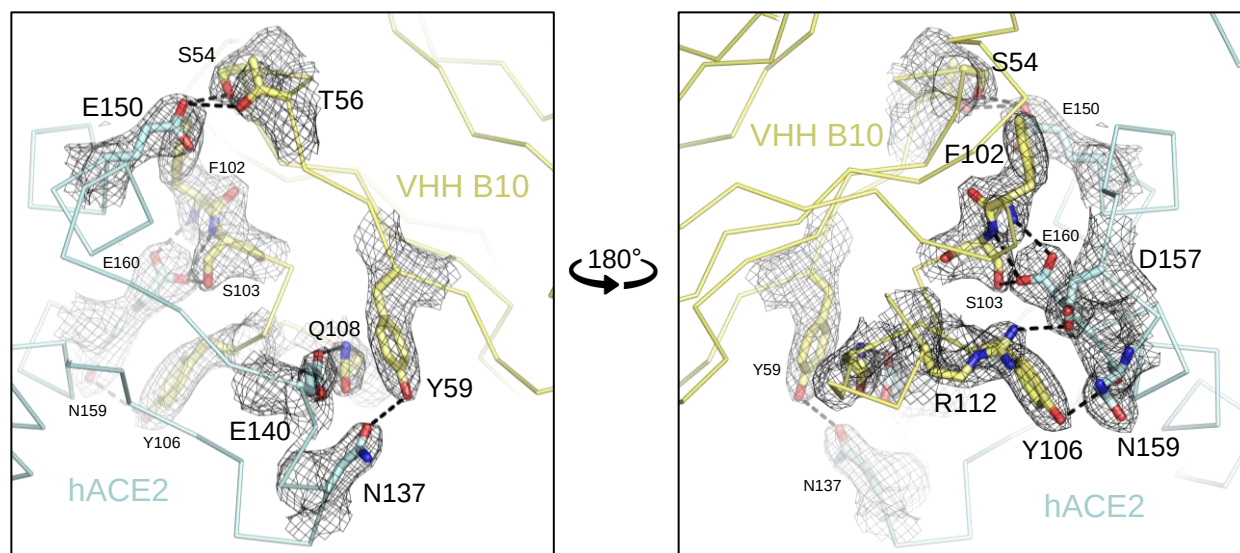
Supplementary Fig. 2: VHH binding on sACE2 and schematic of the binding competition assay. **a** Kinetic analysis of sACE2 on B07-His, B09-His, and B10-His VHHs by BioLayer Interferometry (BLI) using various concentrations of sACE2 (as indicated on the figure). Ni-NTA biosensors were used to immobilize VHH-His. K_D of each VHHs is indicated. One representative experiment out of three. Source Data are provided as a Source Data file. **b** Schematic representation of the binding competition assay. Following a baseline step, the sACE2-Fc (5 $\mu\text{g}/\text{mL}$) was immobilized onto the AHC biosensors. After a second baseline step, a first VHH was applied (VHH1; 5 $\mu\text{g}/\text{mL}$). The sensor was dipped in a mixture of VHH1 + the competitor VHH2 at the same concentration (5 $\mu\text{g}/\text{mL}$).



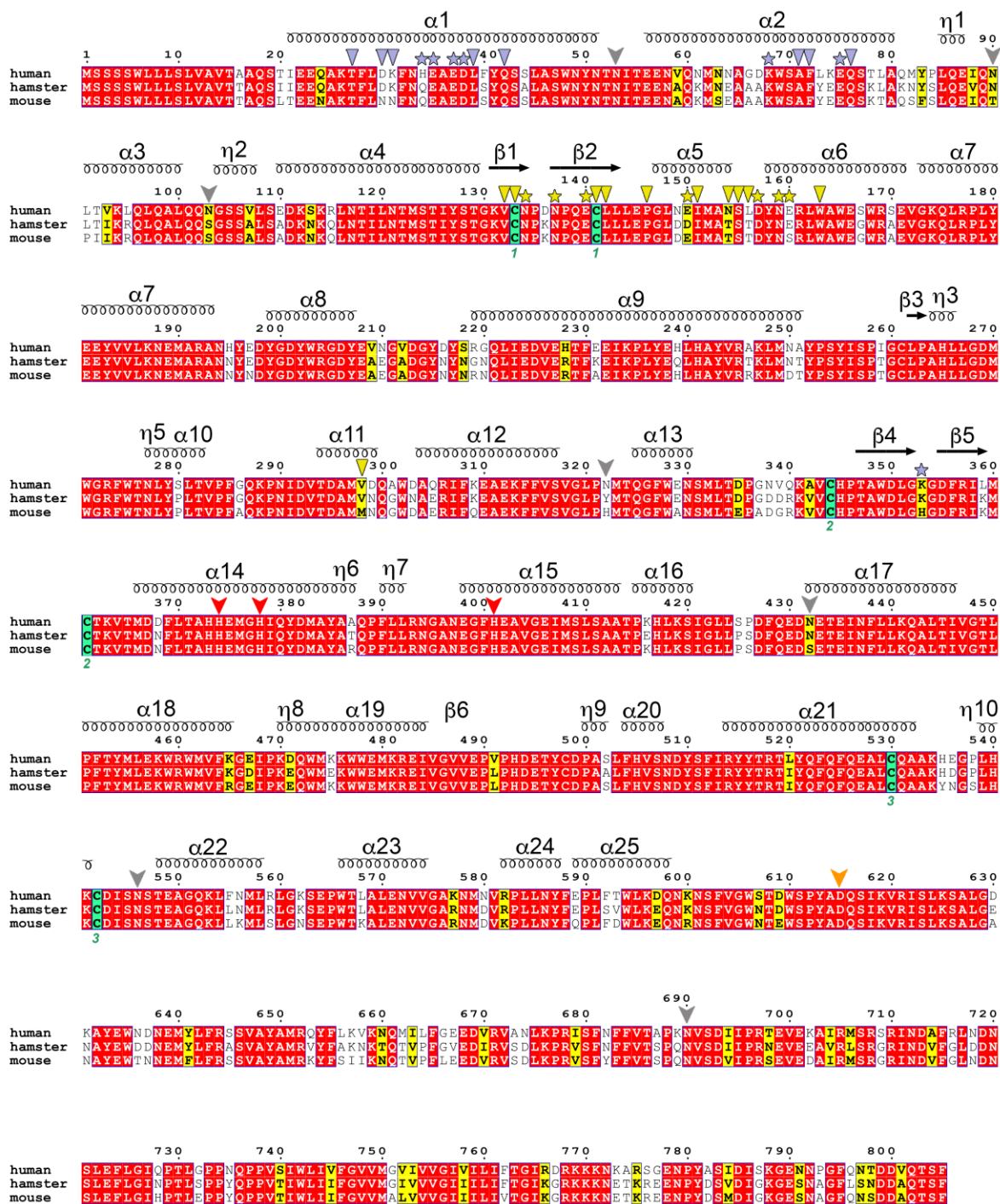
Supplementary Fig. 3: VHHs binding on cells expressing ACE2. **a** Example of FACS sequential gating strategy for detection of hACE2 on cell surface of HEK293-hACE2 cells by VHH or mAbs. **b** ACE2 cell surface detection by the commercial anti-ACE2 antibody AF933 (R&D system, 1 μ g/mL). Data are mean $\pm$ SD of 4 independent experiments. **c** Spike binding to ACE2-expressing cells. Cells were incubated with soluble spike (S) protein (ancestral spike) (10 μ g/mL) and stained with an anti-S antibody. Data are mean $\pm$ SD of 3 independent experiments. **d** B07, B09, and B10 binding on A549-hACE2 (top) and Vero E6 (bottom) cells. Cells were incubated with the VHHs (10 μ g/mL), stained with an anti-myc antibody and a AF488-conjugated anti-mouse antibody, before being analyzed by flow cytometry. Parental A549 cells or myc-tag VHH IgE were used as control. Data are mean $\pm$ SD of 3 (B09, B10); 4 (A549/ B07), or 5 (Vero E6/B07) independent experiments. **e** Fluorescence diagram overlays: B07, B09, B10 efficacy on different cell lines expressing exogenous (A549-hACE2) or endogenous non-human ACE2 (Vero E6). Background (blue) corresponds to the fluorescence intensity obtained on parental cells (A549) or using a VHH control (anti-IgE VHH) (Vero E6). Source Data are provided as a Source Data file.



Supplementary Fig. 4: Interactions between hACE2 and VHH B10. **a** Structure of hACE2/B07/ B10 complex. **b** Rotated view from (a) as indicated and open-book representation of complex hACE2 and VHH B10 (for clarity the VHH B07 was not displayed). The surface of contacts between hACE2 and VHH B10 are displayed in white and contoured in green. The buried surfaces (BSA) are indicated under each surface. **c** Open-book interactions as in (b) with B10 colored complementarity determining regions (CDRs) in green (CDR1), blue (CDR2), and red (CDR3). **d** Detailed interaction between hACE2 and B10 (hydrogen bonds in black dashed lines). **e** Electrostatic potential mapped on the surface of the structure of hACE2 and B10. **f** Impact of hACE2 E160A substitution on B10 binding. Cells were transfected with myc tagged or untagged hACE2 E160A (and eGFP), incubated with an anti-myc antibody or B10 (10 $\mu\text{g/mL}$) and stained with a mouse anti-myc antibody and a AF647-conjugated anti-mouse antibody before being analyzed by flow cytometry. Data are mean of two independent experiments. Source Data are provided as a Source Data file.

a**b**

Supplementary Fig. 5: Experimental 2|Fo|-|Fc| electron density maps at the site of interactions between hACE2 and VHs. For clarity, only the density of the interacting residues, shown as color-coded sticks, is displayed. The maps are contoured at 3 sigma. **a** Two views at 180° each, showing the densities at the site of interactions between hACE2 and VHH B07. **b** Two views at 180° each, showing the densities at the site of interactions between hACE2 and VHH B10.



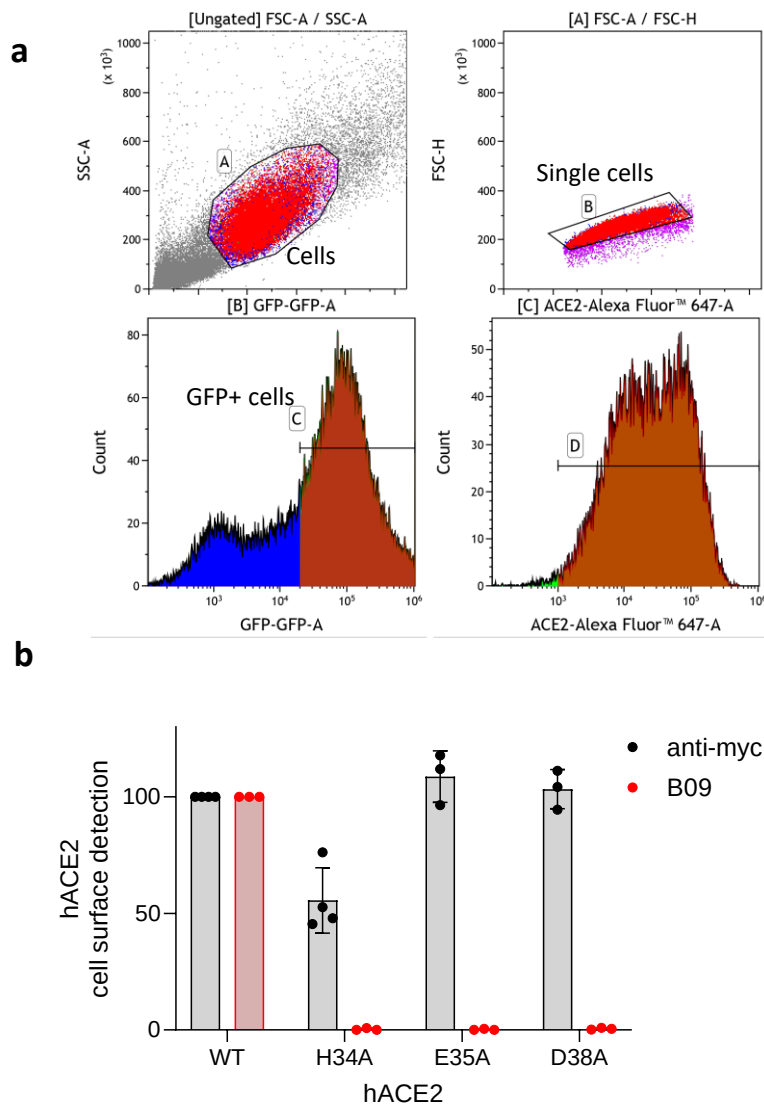
- ▼ glycosylation
- ▼ active site residues
- ▼ last residue seen in X-ray density
- ★ polar interactions hACE2-VHH B07
- ▼ VdW interactions hACE2-VHH B07
- ★ polar interactions hACE2-VHH B10
- ▼ VdW interactions hACE2-VHH B10

red background : amino acid strictly conserved

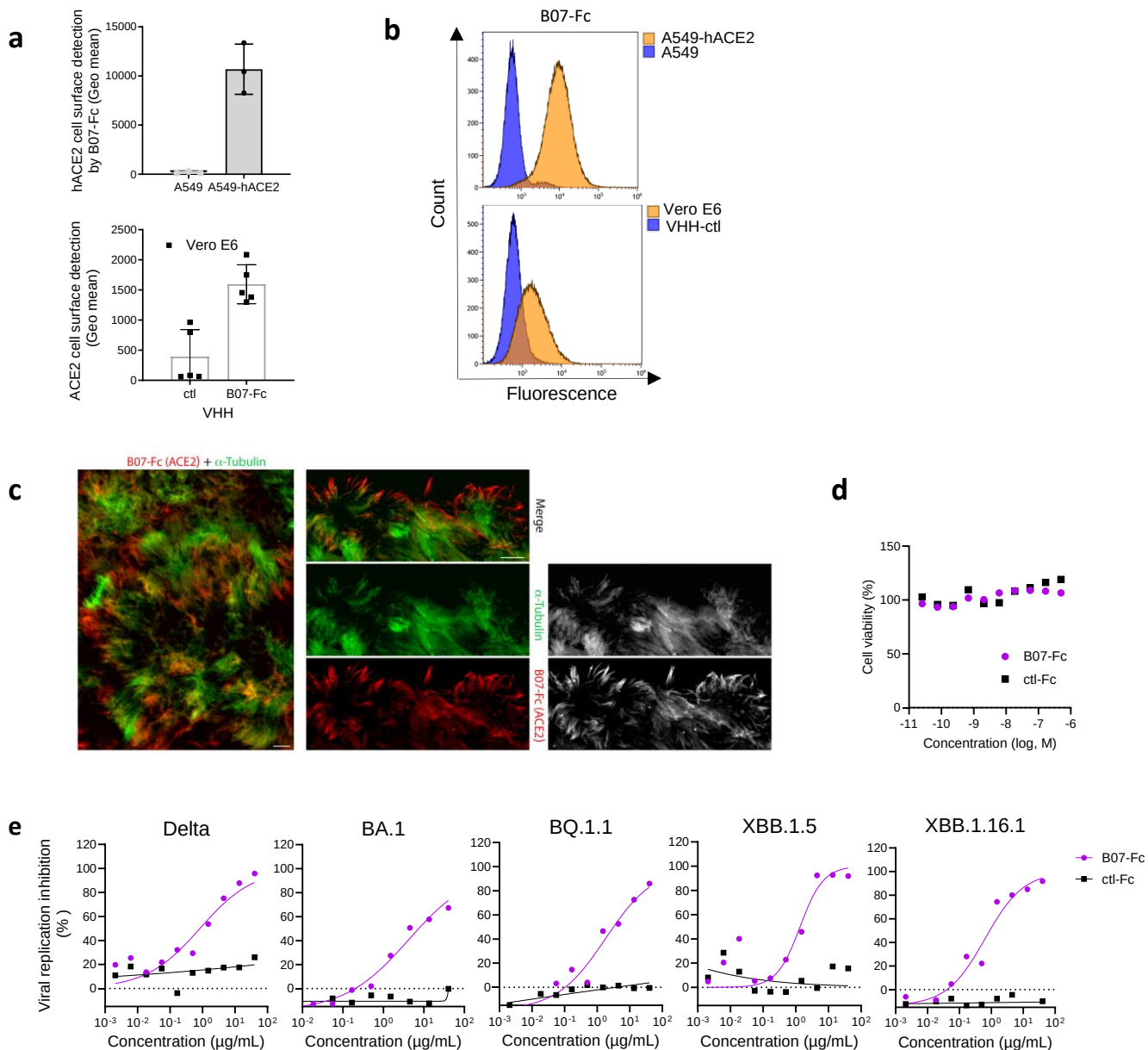
yellow background : amino acid properties conserved (polar, nonpolar)

green background : numbered CYS residues forming disulfide bond

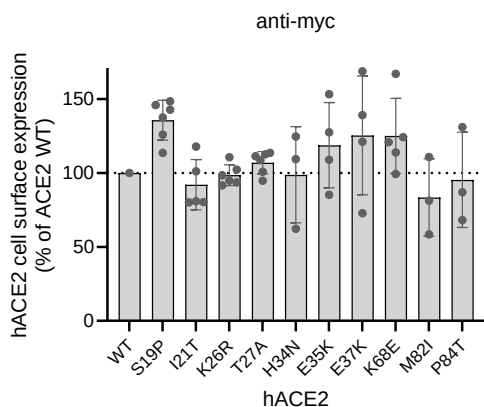
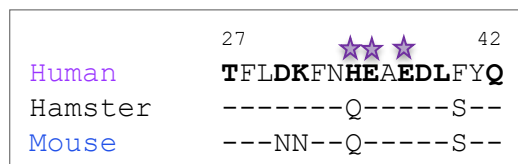
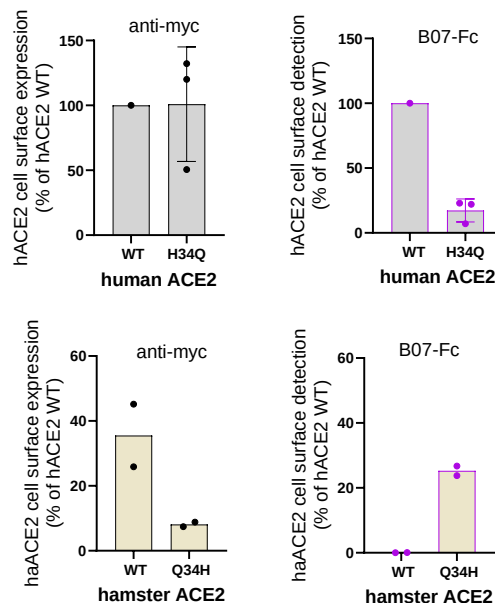
Supplementary Fig. 6: Sequence alignment of human, hamster, and mouse ACE2.



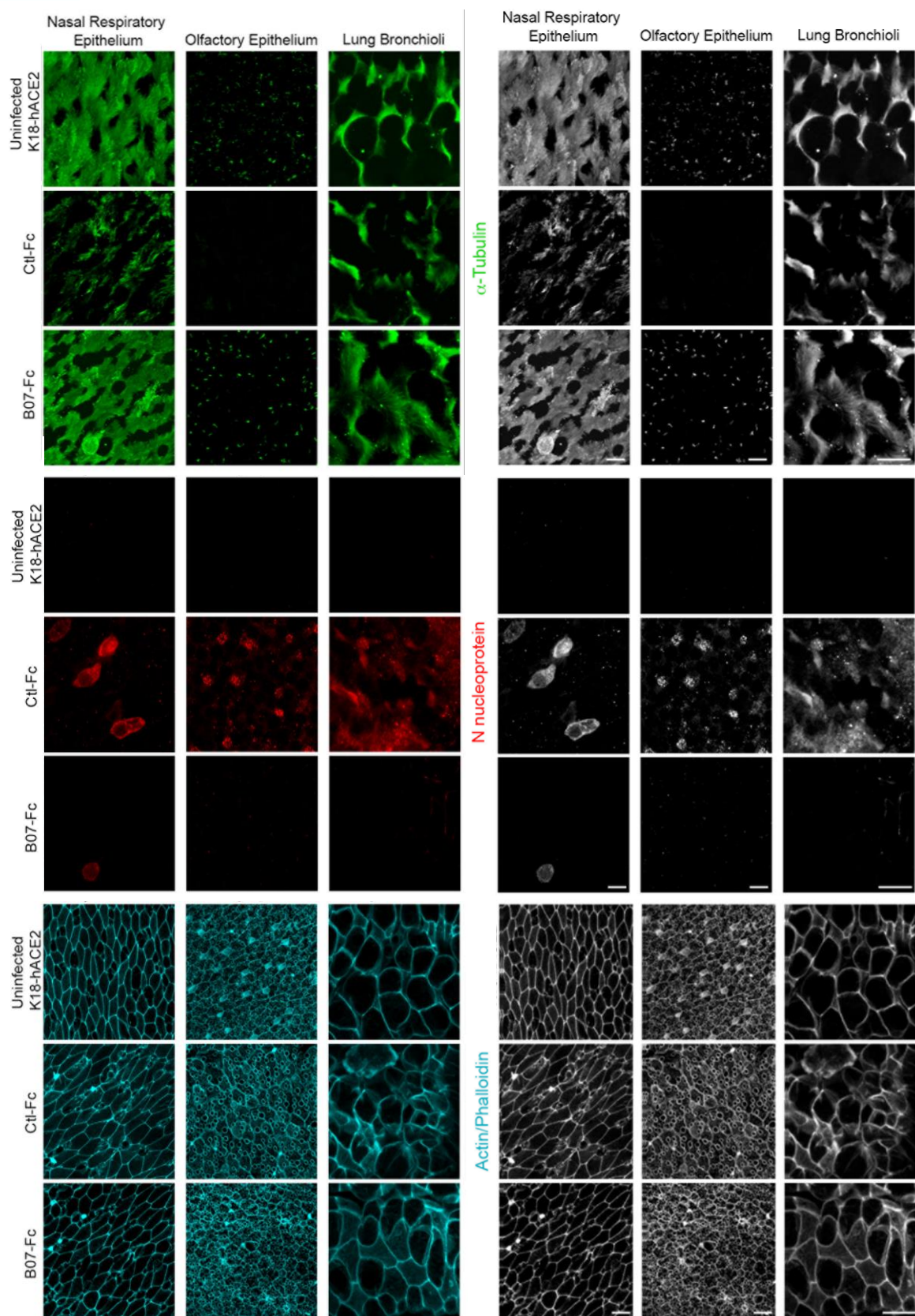
Supplementary Fig. 8: Impact of hACE2 substitution on VHH binding. **a** Example of FACS sequential gating strategy for B07 or anti-myc detection of hACE2 at the cell surface of HEK293 cells co-transfected with plasmids coding hACE2 and eGFP (ratio 5/1, respectively). **b** Impact of alanine substitution on B09 binding. Cells were transfected with untagged or myc tag hACE2 alanine mutants (and eGFP), incubated with an anti-myc antibody or B09 (10 μ g/mL) and stained with a mouse anti-myc antibody and a AF647-conjugated anti-mouse antibody before being analyzed by flow cytometry. Data are mean $\pm$ SD of three (E35A, D38A) or four (H34A) independent experiments. Source Data are provided as a Source Data file.



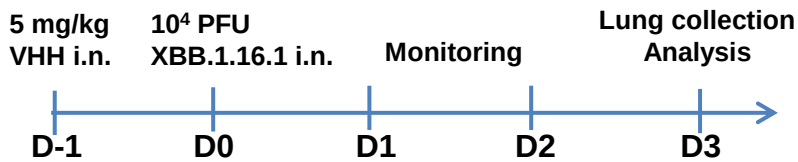
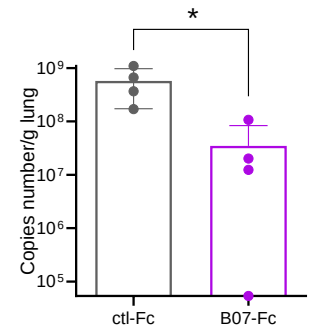
Supplementary Fig. 9: B07-Fc activities. **a** B07-Fc binding on A549-hACE2 and Vero E6 cells. Cells were incubated with 0.1 μ g/mL B07-Fc and a AF488-conjugated secondary antibody, and analyzed as in Fig 6b. Data are mean $\pm$ SD of 3 (A549) or 5 (Vero E6) independent experiments. **b** Fluorescence diagram overlays performed as in Fig. 6c on A549-hACE2 and Vero E6 cells. **c** B07-Fc detection of hACE2 on ciliated cells of human nasal epithelial cells (hNEC). Representative immunofluorescence staining (out of 4 independent experiments) of hACE2 (Red: B07-Fc staining) in combination with α -tubulin (Green). Scale bars: left, 10 μ m; right, 5 μ m. **d** Vero E6 cells viability in the presence of B07-Fc measured by quantitating ATP using the CellTiter-Glo assay (mean of one experiment in triplicates). **e** Inhibition of SARS-CoV-2 replication by B07-Fc measured by RT-qPCR. Vero E6 cells pre-incubated with B07-Fc were infected with Delta B.1.617.2, BA.1, BQ.1.1, XBB.1.5 and XBB.1.16.1 (MOI and incubation time adjusted depending on virus replication, see Methods) and viral replication was measured by quantitative RT-qPCR (mean of one experiment in triplicates). Source Data are provided as a Source Data file.

a**b****c**

Supplementary Fig. 10: Relative cell surface expression of ACE2 mutants and impact of substitutions on B07-Fc binding. HEK293 cells transfected with plasmids encoding myc-hACE2-WT or the indicated mutant were stained with an antibody against the myc epitope or with B07-Fc and analyzed by flow cytometry. **a** Bars represent staining efficiency for cells expressing myc-hACE2 mutants relative to cells expressing myc-hACE2-WT after anti-myc staining. Data are means $\pm$ SD of three (H34N, M82I, P84T), four (E35K, E37K), five (I21T, K68E), or six (S19P, K26R, T27A) independent experiments. **b** Alignment of the amino acid sequences of human, hamster, and mouse ACE2 from position 27 to 42. Residues involved in B07 epitope are in bold. Purple stars indicate polar interactions between hACE2 and B07. **c** Bars represent HEK293 cells transfected with plasmids encoding myc-hACE2 (top) or myc-hamster ACE2 (haACE2, bottom) and stained with an antibody against the myc epitope (left) or with B07-Fc (right) and analyzed by flow cytometry. Data are means $\pm$ SD of three independent experiments (human ACE2), or mean of 2 independent experiments (hamster ACE2). Source Data are provided as a Source Data file.



Supplementary Fig. 11: Separate color (top) or black and white (bottom) images of Fig. 7d. Phalloidin (F-actin), SARS-CoV-2 nucleocapsid (N) (viral replication), and tubulin staining on nasal respiratory epithelium, olfactory epithelium and lung bronchioli extracted from K18-hACE2 uninfected mice, and animals that received VHH-Fc (Ctl-Fc or B07-Fc). Representative immunofluorescence staining of phalloidin (Cyan), SARS-CoV-2 N protein (Red), and tubulin (Green). The staining was performed on nasal, olfactory, and pulmonary epithelium of 2 VHH ctl-treated mice and 4 B07-Fc treated mice. Scale bars: 10 μ m.

a**b**

Supplementary Fig. 12: Effect of VHH B07-Fc on hamsters. **a** Schematic diagram showing the experimental design of B07-Fc prophylaxis in XBB.1.16.1 infected hamsters. Animals received intranasally (i.n.) 5 mg/kg VHH-B07-Fc (B07-Fc) or 5 mg/kg VHH-Fc ctl (ctl-Fc). Twenty four hours later, they were infected with 10⁴ PFU XBB.1.16.1 intranasally (i.n.). Three days post-infection, lungs were collected for analysis. Animal behavior and weight were followed each day. **b** RNA load measured by RT-qPCR of SARS-CoV-2 in lung. Data are mean $\pm$ SD of 4 animals. Mann-Witney test (two-tailed): P value 0.0286*. Source Data are provided as a Source Data file.

a	B07			B09		
		P values CI ($\mu\text{g/mL}$)	R^2		P values CI ($\mu\text{g/mL}$)	R^2
	Delta	16.97 to 51.41	0.8712	Delta	12.39 to 26.22	0.8901
	BA.1	8.563 to 23.63	0.8616	BA.1	17.52 to 41.94	0.9223
	BQ.1.1	3.885 to 6.914	0.9890	BQ.1.1	4.839 to 12.49	0.9711
	XBB1.5	6.116 to 13.25	0.9192	XBB1.5	6.435 to 10.67	0.9669
	XBB.1.16.1	4.261 to 6.938	0.9909	XBB.1.16.1	8.562 to 16.19	0.9815
	EG.5.1.3	2.628 to 3.891	0.9948	EG.5.1.3	4.643 to 12.95	0.9631
	BA.2.86.1	0.7223 to 2.903	0.9412	BA.2.86.1	1.300 to 8.622	0.8942

b	VHH	Delta	BA.1	BQ.1.1	XBB.1.5	XBB.1.16.1	EG.5.1.3	BA.2.86.1
	B07	1937.2	932.8	339.8	590.4	356.9	209.9	95.1
	B09	1180.7	1776.3	509.1	543.2	771.2	507.8	219.5
	B10	-	-	-	-	-	-	-
	Ctl	-	-	-	-	-	-	-
		IC50 (nM)						

c	S-Fuse			Anti-N		
		p-values CI ($\mu\text{g/mL}$)	R^2		p-values CI (ng/mL)	R^2
	Delta	0.1714 to 0.3072	0.9702	JN.1.1	3.71 to 5.50	0.9928
	BA.1	0.1603 to 0.2168	0.9891	KP.3.3	5.45 to 6.56	0.9966
	BQ.1.1	0.09368 to 0.1397	0.9761			
	XBB1.5	0.07860 to 0.1756	0.9420			
	XBB.1.16.1	0.08340 to 0.1088	0.9908			
	EG.5.1.3	0.06759 to 0.08863	0.9923			
	BA.2.86.1	0.07032 to 0.1454	0.9546			
	JN.1.1	0.1222 to 0.1561	0.9862			
	KP3.3	0.2897 to 0.3875	0.9801			

Supplementary Table 1: Statistical analyses and IC50 related to Fig. 4a and 6g (S-Fuse assay), and 6h (N detection). **a** P-values 95% confidence intervals for VHH IC50 values and R^2 values relative to B07 and B09 IC50s (Fig. 4a). Curves were fitted with a non-linear regression model (variable slope). **b** B07 IC50 values in nM (Fig. 4a). **c** P-values 95 % confidence intervals and R^2 values relative to B07-Fc IC50 obtained in S-Fuse (Fig. 6g) or inhibition infection (anti-N) assays (Fig. 6h). Curves were fitted with a non-linear regression model (variable slope). Source Data are provided as a Source Data file.

hACE2 - VHH B07 - VHH B10	
Data collection[£]	
Space group	P 1 2 ₁ 1
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	97.9, 108.1, 146.1
α , β , γ (°)	90, 98.9, 90
High resolution (Å) cut-off at CC _{1/2} >30%	2.69
Resolution (Å)	48.37-2.69 (2.76-2.69)
Rmerge (all I+ & I-) (%)	23.6 (159)
Rmeas (all I+ & I-) (%)	25.5 (171.5)
Rpim (all I+ & I-) (%)	9.5 (63.6)
Measured reflections	590,491 (43,028)
Unique reflections	83,613 (6,015)
<I/σI>	9.2 (1.3)
Completeness (%)	99.8 (97)
Multiplicity	7.1 (7.2)
CC _{1/2} (%)	99.2 (37.5)
B-Wilson (Å ²)	63.8
Number of molecules/asymmetric unit	3x(ACE2 - VHH B07 - VHH B10)
Refinement[£]	
Resolution	48.3-2.69 (2.71-2.69)
Number of reflections Work/Free	83,594 (1,589) / 4,180 (83)
Rwork (%) / Rfree (%)	21.9 (34.1) / 25.4 (39.1)
Root mean square deviation	
Bond lengths (Å)	0.007
Bond angles (°)	0.87
No. of atoms	
Protein	20,123
Solvent	104
Chloride ions	4
Glycans	13
B-mean (Å ²) (all atoms)	70.2
Ramachandran (%) ^{\$}	
Favoured / Allowed / Outliers	97 / 2.88 / 0.12

[£] Values in parentheses are for the highest-resolution shell

^{\$} Ramachandran statistics were calculated with MolProbity

Supplementary Table 2: Crystallization conditions, data collection and refinement statistics.

Residues in hACE2 and VHH B10 involved in van der Waals contacts

hACE2	ss	H/S	ASA (Å ²)	BSA (Å ²)	ΔiG (kcal/mol)
VAL 132	β1		1.74	1.23	-0.01
CYS 133	β1		37.99	1.28	0.02
ASN 134	β1		59.59	27.51	-0.23
ASN 137	β2	H	61.75	16.45	-0.28
GLU 140	β2	H	103.32	79.65	-0.41
CYS 141	β2		37.18	3.08	0.05
LEU 142	β2		57.57	32.86	0.52
PRO 146	loop β2-α5		83.77	2.68	0.04
GLU 150	α5	H	111.20	74.53	-0.51
ILE 151	α5		25.26	24.42	0.39
ASN 154	α5		110.53	43.86	0.29
SER 155	loop α5-α6		14.63	12.32	0.15
LEU 156	loop α5-α6		122.74	70.82	1.01
ASP 157	loop α5-α6	HS	71.03	54.04	0.09
ASN 159	α6	H	89.83	23.87	0.24
GLU 160	α6	H	75.85	75.85	-0.26
TRP 163	α6		107.99	51.76	0.81
VAL 298	α11		93.84	4.66	0.07

VHH B10	CDR	H/S	ASA (Å ²)	BSA (Å ²)	ΔiG (kcal/mol)
THR 28	FR1		72.00	6.86	0.11
SER 30	FR1		55.90	1.47	-0.02
SER 31	CDR1		53.24	34.54	0.28
TYR 32	CDR1		55.51	23.51	0.04
SER 52	CDR2		4.26	2.25	0.03
SER 54	CDR2	H	54.21	10.68	0.08
THR 56	CDR2	H	125.88	16.31	-0.14
SER 57	CDR2		48.79	10.31	-0.00
TYR 59	CDR2	H	98.43	39.18	0.28
ALA 75	FR3		98.79	4.67	0.07
LYS 100	CDR3		92.82	28.85	0.07
GLY 101	CDR3		21.23	21.06	0.34
PHE 102	CDR3	H	98.61	95.00	1.38
SER 103	CDR3	H	36.15	29.79	0.33
THR 104	CDR3		14.96	4.54	-0.05
ILE 105	CDR3		151.17	138.96	1.99
TYR 106	CDR3	H	151.51	89.10	0.91
ASN 107	CDR3		0.62	0.62	-0.01
GLN 108	CDR3	H	58.04	16.87	-0.28
ARG 112	CDR3	HS	54.59	26.41	-0.67

Polar contacts between hACE2 and VHH B10

hACE2				VHH B10	
atom	ss	distance (Å)		atom	CDR
ASN 137 OD1	β2	H	3.61	TYR 59 OH	CDR2
GLU 140 OE2	β2	H	3.40	GLN 108 NE2	CDR3
GLU 150 OE2	α5	H	2.83	SER 54 OG	CDR2
GLU 150 OE2	α5	H	3.36	THR 56 OG1	CDR2
ASP 157 OD2	α6	HS	3.63	ARG 112 NH1	FR4
ASP 157 OD2	α6	HS	2.93	ARG 112 NH2	FR4
ASN 159 O	α6	H	3.57	TYR 106 OH	CDR2
GLU 160 OE1	α6	H	2.58	SER 103 OG	CDR3
GLU 160 OE1	α6	H	3.10	SER 103 N	CDR3
GLU 160 OE2	α6	H	2.88	PHE 102 N	CDR2

Supplementary Table 3: Van der Waals and polar interactions between hACE2 and VHH B10. CDR: complementary-determining region (KABAT definition); FR: Framework region; ss: secondary structure in hACE2; H: hydrogen bonds; S: salt-bridges; ASA: accessible surface area; BSA: buried surface area; ΔGi: solvation energy effect; Vertical bars in BSA columns indicate the buried area percentage (with one bar per 10% of ASA).

Residues in hACE2 and VHH B07 involved in van der Waals contacts

hACE2	SS	HS	ASA (Å ²)	BSA (Å ²)	ΔiG (kcal/mol)	VHH B07	CDR	HS	ASA (Å ²)	BSA (Å ²)	ΔiG (kcal/mol)
THR 27	a1		71.69	13.25	0.20	SER 30	FR1		58.84	1.96	-0.02
ASP 30	a1		99.65	18.60	0.23	THR 31	CDR1		101.13	52.93	0.21
LYS 31	a1		121.90	48.19	0.77	ASN 32	CDR1	H	40.87	21.48	-0.26
HIS 34	a1	H	139.56	120.57	0.60	THR 33	CDR1	H	50.34	47.92	-0.09
GLU 35	a1	HS	85.73	79.49	-0.32	TYR 37	FR2		8.16	1.11	-0.01
GLU 37	a1	H	81.81	46.14	-0.54	LEU 47	FR2		55.19	25.76	0.41
ASP 38	a1	H	80.63	77.51	-0.25	SER 50	CDR2		17.02	16.04	0.07
LEU 39	a1		44.52	33.13	0.53	ILE 51	CDR2		11.20	0.33	0.01
GLN 42	a1		94.45	48.95	-0.11	SER 52	CDR2		29.38	29.38	0.43
LYS 68	a2	H	121.21	51.24	-0.91	THR 53	CDR2	H	62.84	34.94	-0.20
ALA 71	a2		62.37	25.40	0.31	SER 54	CDR2	H	93.93	22.99	0.24
PHE 72	a2		14.52	14.52	0.21	ASN 56	CDR2	H	112.21	21.83	0.03
GLU 75	a2	HS	94.37	54.58	-0.29	THR 57	CDR2		74.73	3.97	0.01
GLN 76	a2		8.80	2.04	-0.02	TYR 58	CDR2		127.07	101.47	0.73
LYS 353	loop b4-b5	H	119.29	28.47	-0.85	PRO 60	CDR2		26.45	1.84	0.03
						PRO 98	CDR3		43.13	39.61	0.63
						SER 99	CDR3		71.98	55.05	-0.16
						ARG 101	CDR3	HS	84.80	53.72	-1.48
						ILE 102	CDR3		138.09	84.75	1.36

Polar contacts between hACE2 and VHH B07

hACE2				VHH B07	
atom	SS	distance (Å)		atom	CDR
HIS 34 NE2	a1	H	3.12	ASN 56 O	CDR2
GLU 35 OE1	a1	HS	3.01	ARG 101 NH1	CDR3
GLU 35 OE2	a1	HS	2.90	ARG 101 NH2	CDR3
GLU 37 OE1	a1	H	3.75	ASN 56 ND2	CDR2
GLU 37 OE1	a1	H	3.40	SER 54 OG	CDR2
ASP 38 OD1	a1	H	2.76	THR 53 OG1	CDR2
ASP 38 OD2	a1	H	2.79	THR 33 OG1	CDR1
ASP 38 OD2	a1	H	3.05	THR 53 N	CDR2
LYS 68 NZ	a2	H	3.26	ASN 32 OD1	CDR1
GLU 75 OE1	a2	HS	3.07	ARG 101 NE	CDR3
GLU 75 OE2	a2	HS	2.89	ARG 101 NH1	CDR3
LYS 353 NZ	loop b4-b5	H	2.79	THR 53 OG1	CDR2

Supplementary Table 4: Van der Waals and polar interactions between hACE2 and VHH B07. CDR: complementary-determining region (KABAT definition); FR: Framework region; ss: secondary structure in hACE2; H: hydrogen bonds; S: salt-bridges; ASA: accessible surface area; BSA: buried surface area; ΔGi: solvation energy effect; Vertical bars in BSA columns indicate the buried area percentage (with one bar per 10% of ASA).

hACE2		hACE2/VHH B07-B10 (this work)		hACE2/RBD SARS CoV-2 (PDB 6M0J)		hACE2/RBD SARS CoV (PDB 2AJF)		hACE2/RBD HCoV-NL63 (PDB 3KBH)	
residues	ss	HS	BSA (Å ²) VHH B07	HS	BSA (Å ²) RBD	HS	BSA (Å ²) RBD	HS	BSA (Å ²) RBD
SER 19	N-ter				10.86		31.48		
GLU 23	α 1						1.24		
GLN 24	α 1			H	54.04	H	39.35		
THR 27	α1		13.25 		67.91 		73.41 		
PHE 28	α 1				14.77		11.99		
ASP 30	α1		18.60 	HS	41.36 		13.25 		22.50
LYS 31	α1		48.19 		91.32 		52.47 		3.56
ASN 33	α 1								20.55
HIS 34	α1	H	120.57 	H	74.52 		62.39 		61.01
GLU 35	α1	HS	79.49 	H	14.69 				
GLU 37	α1	H	46.14 	H	14.30 	H	17.13 	H	37.61
ASP 38	α1	H	77.51 	H	32.56 	H	34.28 		1.97
LEU 39	α 1		33.13			H			
TYR 41	α 1			H	42.44	H	44.99	H	35.07
GLN 42	α1		48.95 	H	46.41 	H	32.19 		
LEU 45	α 1				27.84		33.41		
LYS 68	α 2	H	51.24						
ALA 71	α 2		25.40						
PHE 72	α 2		14.52						
GLU 75	α 2	HS	54.58						
GLN 76	α 2		2.04						
LEU 79	α 2				25.95		31.12		
MET 82	α 2- η 1				27.86		37.04		
TYR 83	α 2- η 1			H	36.50	H	31.15		
PRO 321	α 12- α 13								19.46
ASN 322	α 12- α 13								12.31
MET 323	α 12- α 13								1.96
THR 324	α 12- α 13				2.18		5.02	H	44.17
GLN 325	α 13				8.02	H	43.00		42.15
GLY 326	α 13				2.01		13.88		19.16
GLU 329	α 13					HS	27.64		
ASN 330	α 13				28.75	H	33.10		15.67
LYS 353	loop β4-β5	H	28.47 	H	98.99 	H	104.54 	H	65.15
GLY 354	β 5				30.22		27.83		54.04
ASP 355	β 5				12.29		10.29		15.47
PHE 356	β 5								10.01
ARG 357	β 5				12.01		10.82		3.79
MET 383	α 14								30.27
ALA 384	α 14								1.90
ALA 386	α 14				0.25				23.96
ALA 387	α 14							H	40.36
PRO 390	η 7								1.57
ARG 393	η 7- α 15			H	10.70		6.70		23.51
PHE 555	α 22								10.92

Supplementary Table 5: Van der Waals contacts between hACE2 and VHH B07 and between hACE2 and RBDs for a selection of viruses using hACE2 as a receptor. ss: secondary structure of hACE2; H: hydrogen bonds; S: salt-bridges; BSA: buried surface area; Vertical bars in BSA columns indicate the buried area percentage (with one bar per 10% of ASA of each indicated residue). In bold red are indicated the common interactions between B07 and SARS-CoV-2 RBD structures. In bold red italic are indicated the common interactions between the four structures.