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## **Supplemental Information**

# HCV Broadly Neutralizing Antibodies Use a CDRH3

### **Disulfide Motif to Recognize an E2 Glycoprotein**

### Site that Can Be Targeted for Vaccine Design

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**Figure S1. The schematic representation of HCV polyprotein (A) and HCV E2 (B).** E2 regions are colored by structural components: HVR1 (orange), AS412 (dark green), front layer (yellow), VR2 (red), ß-sandwich (violet), CD81bl (blue), VR3 (light grey), post-VR3 (dark grey), back layer (green), and stem (black). Related to introduction and Figure 2.



**Figure S2. Sequence alignments of HEPC3 (A), HEPC74 (B), or AR3C (C) CDRH3 sequences with potential germline precursor genes.** Dots indicated identical amino acids and dashes indicate regions encoded by other gene segments or N-nucleotide additions. Two cysteines in CDRH3 are highlighted in bold. The two most likely D-gene segments for AR3C are indicated. Related to Figure 1.



**Figure S3. Comparison of HEPC3, HEPC74, and AR3C structures in unliganded and bound states.** Superposition of unliganded (colored) and bound (grey) Fab structures of HEPC3 (A), HEPC74 (B), or AR3C (C) (PDB 4MWF for the AR3C-bound Fab structure). The Fabs were superimposed on their V<sub>H</sub> domains. Protein backbones are shown as ribbons and CDR loops are blue (CDRH1), orange (CDRH2), and red (CDRH3). Disulfide bonds are shown as yellow sticks. Related to Figure 3, 4.



Figure S4. Comparison of E2core and E2ecto structures. Superposition of  $E2core_{1a53}$  (grey) and  $E2ecto_{1b09}$  (wheat) (A);  $E2core_{1a53}$  (grey) and  $E2ecto_{1a53}$  (light blue) (B); and  $E2ecto_{1b09}$  (wheat) and  $E2ecto_{1a53}$  (light blue) (C) structures. Rmsds calculated for superposition of 168 C $\alpha$  atoms between the E2core and E2ecto structures (A-B) and 189 C $\alpha$  atoms between the E2ecto structures (C). The HVR1, AS412, and VR2 regions were omitted from the rmsd calculations. Protein backbones are shown as ribbons and disulfide bonds are shown as yellow sticks. Related to Figure 5.



Figure S5. The structure of E2core<sub>1a53</sub> in complex with HEPC46. Cartoon representation of the crystal structure of HEPC3-E2core<sub>1a53</sub>-HEPC46 complex (HEPC3 Fab not shown for clarity). E2core is colored according to structural elements: Front layer (yellow),  $\beta$ -sandwich (violet), CD81bl (blue), VR3 (light grey), post-VR3 (dark grey), and back layer (green). HEPC46-HC is dark blue and HEPC46-LC is light blue. Disulfide bonds are shown as yellow sticks; dashed lines indicate disordered regions. Related to Figure 2.



Figure S6. Binding of HEPC3, HEPC74, AR3C and their germline precursors to a panel of

**19 genotype 1 E2ecto proteins.** Values shown are means  $\pm$  s.d. of duplicates. One experiment representative of two independent experiments is shown. Related to Figure 7.



Figure S7. Neutralization capacity of HEPC3, HEPC74, AR3C and their germline precursors against a panel of genotype 1 HCVpp. Values shown are means  $\pm$  s.d. of duplicates. Related to Figure 7.

#### Table S1 Data collection and refinement statistics for unliganded Fab structures.

Related to Figure 1 and Figure S3.

	HEPC3	HEPC74	AR3C	HEPC46
Data collection				
Wavelength (Å)	1.19	0.98	1.00	0.98
Resolution range (Å)	38.32 - 2.04 (2.11 - 2.04)	33.55 - 1.36 (1.41 - 1.36)	54.28 - 2.90 (3.00 - 2.90)	32.28 - 1.41 (1.46 - 1.41)
Space group	P22 <sub>1</sub> 2 <sub>1</sub>	P1	1222	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Cell, Å (a, b, c)	98.91, 108.69 166.25	55.13, 63.59, 73.76	76.67, 146.87, 175.25	54.64, 71.30, 108.59
Angles (α, β, γ)	90, 90, 90	80, 74, 84	90, 90, 90	90, 90, 90
Total reflections	502,575 (49,122)	1,209,301 (119,316)	129,013 (13,533)	402,422 (40,082)
Unique reflections	114,386 (11,299)	190,820 (18,843)	22,311 (2,207)	81,622 (8,076)
Multiplicity	4.4 (4.3)	6.3 (6.3)	5.8 (6.1)	4.9 (5.0)
Completeness (%)	99.9 (99.8)	93.7 (92.4)	99.5 (99.5)	99.0 (99.7)
l/σl	9.17 (1.50)	11.54 (1.41)	8.03 (1.12)	11.10 (1.71)
Wilson B-factor (Å <sup>2</sup> )	32.35	17.62	75.33	16.43
R <sub>merge</sub> (%)	10.16 (95.94)	6.77 (120.80)	16.67 (170.3)	6.40 (81.06)
R <sub>pim</sub> (%)	5.35 (51.08)	2.83 (51.48)	7.55 (74.81)	3.07 (39.19)
CC <sub>1/2</sub>	99.7 (55.7)	99.9 (48.7)	98.9 (52.8)	99.8 (66.6)
Refinement statistics				
R <sub>work</sub>	18.13	16.75	22.14	17.46
R <sub>free</sub>	21.60	19.08	25.45	20.08
Number of atoms	10,921	7,996	3,290	3,821
Protein	9,889	6,592	3,290	3,224
Ligands	30	-	-	-
Solvent	1,002	1,404	-	597
Protein residues	1,305	873	436	432
R.m.s deviations				
Bond lengths (Å)	0.011	0.009	0.011	0.009
Bond angles (°)	1.36	1.06	1.53	1.05
Clashscore	3.94	4.06	11.09	5.03
Average B-factor	36.94	26.6	78.15	24.95

Numbers in parentheses correspond to the highest resolution shell

Table S2 Data collection and refinement statistics for bNAb Fab-E2 complexes. Related to Figure 2 and Figure 5.

	HEPC74-E2ecto <sub>1b09</sub>	HEPC3-E2ecto <sub>1b09</sub>	HEPC3-E2ecto <sub>1a53</sub> -HEPC46	HEPC3-E2core <sub>1a53</sub> -HEPC46
Data collection				
Wavelength (Å)	0.98	1.00	1.00	0.98
Resolution range (Å)	43.76 - 1.99 (2.06 - 1.99)	69.48 - 2.90 (3.00 - 2.90)	78.27 - 2.80 (2.90 - 2.80)	76.97 - 3.10 (3.21 - 3.10)
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	P21	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Cell, Å (a, b, c)	66.31, 69.77, 168.58	65.81, 75.79, 174.00	86.44, 76.64, 118.26	75.40, 105.59, 337.28
Angles (α, β, γ)	90, 90, 90	90, 90, 90	90, 106, 90	90, 90, 90
Total reflections	317,277 (24,655)	104,643 (10,272)	114,902 (10,691)	524,186 (44,182)
Unique reflections	53,843 (4,890)	19,947 (1,968)	36,828 (3,637)	49,943 (4,864)
Multiplicity	5.9 (5.0)	5.2 (5.2)	3.1 (2.9)	10.5 (9.1)
Completeness (%)	98.6 (90.9)	98.6 (100.0)	99.7 (99.1)	99.9 (99.7)
l/σl	7.32 (1.36)	6.50 (3.40)	6.81 (1.35)	12.72 (2.31)
Wilson B-factor (Å <sup>2</sup> )	36.03	37.76	64.73	77.54
R <sub>merge</sub> (%)	11.15 (86.45)	17.81 (29.37)	10.75 (74.46)	13.84 (88.36)
R <sub>pim</sub> (%)	4.96 (47.49)	8.87 (14.03)	7.25 (51.38)	4.44 (30.41)
CC <sub>1/2</sub>	95.9 (29.7)	96.9 (93.2)	98.3 (79.6)	99.7 (78.0)
Refinement statistics				
Rwork	18.62	20.98	19.88	22.4
R <sub>free</sub>	22.98	27.53	27.10	29.0
Number of atoms	5,089	5,589	8,500	15,747
Protein	4,588	5,202	8,333	15,435
Ligands	98	183	167	312
Solvent	403	204	-	-
Protein residues	603	693	1,099	2,044
R.m.s deviations				
Bond lengths (Å)	0.008	0.007	0.010	0.008
Bond angles (°)	1.29	1.25	1.49	1.35
Clashscore	4.02	8.56	16.39	15.53
Average B-factor	50.9	32.04	75.1	76.9

Numbers in parentheses correspond to the highest resolution shell

Table S3. HEPC3 and AR3C interfaces with E2cores. Shared E2core contact residues and hydrogen bonds are shaded grey.	
Data for the AR3C-E2core1a154 complex was derived from PDB 4MWF. Related to Figure 2.	

List of HE	EPC3 heavy chain (	chain H)-E2	core <sub>1a53</sub> (chain C) interfa	ice residues	List of A	AR3C heavy chain	(chain H)-E2cc	ore <sub>1a154</sub> (chain C) interfac	e residues
(the	e residues on each	row are not	matched interactive pa	rtners)	(th	ne residues on eac	h row are not i	matched interactive part	ners)
H'GLN 1	Bollu	68 68	C:1 ELL 427	49	H-ASP 30	BUIIU	40	C:II E 422	40
H:VAL 2	н	17	C:ASN 428	25	H:ASN 31		7	C:THR 425	2
H:GLY 27		15	C:CYS 429 H	35	H:TYR 32	н	33	C:LEU 427 H	74
H:THR 28	Н	101	C:ASN 430	22	H:VAL 52		3	C:ASN 428	11
H:LEU 29		78	C:ASP 431 HS	37	H:LEU 53		60	C:CYS 429 H	35
H:ASN 30 H:SER 31	н	60	C:SER 432	12	H:PHE 54		97	C:ASN 430	14
H:TYR 32		5	C:ASN 434 H	134	H:VAL 96		11	C:SER 432 H	18
H:GLU 33		11	C:THR 435 H	60	H:THR 97	н	48	C:LEU 433	48
H:THR 52		14	C:GLY 436	36	H:PRO 98		62	C:GLY 436	23
H:PRO 53		45	C:TRP 437	13	H:ARG 99	Н	87	C:LEU 438	45
H:ILE 54		47	C:LEU 438	42	H:TYR 100		30	C:ALA 439	28
H:PHE 55	нс	5 10	C:GLX 439	52 11	H:CYS 100A	н	80	C:LEU 441	22
H:SER 76	110	1	C:PHE 442	30	H:GLY 100C	н	59	C:TYR 443 H	112
H:ARG 94	HS	35	C:TYR 443	89	H:GLY 100D		28	C:GLN 444	2
H:VAL 97		59	C:HIS 444	5	H:CYS 100F		6	C:LYS 446	12
H:ARG 98	н	96	C:HIS 445	3				C:TRP 529	78
H:TYR 99		36	C:LYS 446 HS	134				C:ALA 531	9
H:CYS 100	Н	78	C:PHE 447 H	45				C:TYR 613	9
HIGLY 100A		14	C:ASP 448 H	63					
H:GLY 100B		59	C:GLU 531	42					
H:CYS 100E		32	0.0L0 331	22					
H:ASP 101	н	7							
H:PRO 102		4							
Total		959		1000	Total		671	Total	704
	Hydrog	en bonds		_		Hydro	gen bonds		-
##	Heavy chain	Distance (A)	) E2core <sub>1a53</sub>	-	##	Heavy chain	Distance (A)	E2core <sub>1a154</sub>	-
1	H:CYS 100[ O ]	3.1	C:CYS 429[ N ]		1	H:ARG 99[0]	3.5	C:GLU 431[ N ]	
3		3.2	C:ASP 43 I[ N ]		3		3.2	C:SER 432[N]	
4	H:GLU 73[ OE2]	2.9	C:LYS 446[ NZ ]		4	H:TYR 32[ N ]	3.4	C:TYR 443[ OH ]	
5	H:THR 28[ O ]	2.7	C:ASP 448[ N ]		5	H:THR 97[N]	3.5	C:TYR 443[ OH ]	
6	H:CYS 100[ N ]	2.9	C:CYS 429[ O ]		6	H:ARG 99[NH1]	3.6	C:SER 432[ O ]	
7	H:ARG 98[ NE ]	2.8	C:ASP 431[ O ]		7	H:ARG 99[ NH1]	3.5	C:SER 432[ OG ]	
8	H:ARG 94[ NH1]	3.9	C:ASP 431[ OD2]		8	H:CYS 100A[ N ]	2.7	C:CYS 429[O]	
9	H:VAL 2[ N ]	3.0	C:ASN 434[ O ]		9	H:GLY 100C[ N ]	3.6	C:LEU 427[ O ]	
10	H:ARG 94[ NH 1]	2.3	C:ASN 434[ OD 1]						
12	H:ASN 30[ N ]	2.8	C:LYS 446[ O ]						
13	H:ASN 30[ ND2]	3.3	C:PHE 447[ O ]						
	Salt b	oridges		-		No salt b	ridges observ	ed	-
##	Heavy chain	Distance (Å)	) E2core <sub>1a53</sub>	_			0		-
1	H:GLU 73[ OE1]	2.8	C:LYS 446[ NZ ]						
2	H:GLU 73[ OE2]	2.9	C:LYS 446[ NZ ] C:ASP 431[ OD2]						
		0.0							
List of H	EPC3 light chain (c	row are not	ore <sub>1a53</sub> (chain C) interface matched interactive na	ce residues	List of	AR3C light chain (	chain L)-E2co	re <sub>1a154</sub> (chain C) interface	e residues
Light chain	Bond	BSA (Å <sup>2</sup> )	E2core1a53 Bond	BSA (Å <sup>2</sup> )	Light chain	Bond	BSA (Å <sup>2</sup> )	E2core1a154 Bond	BSA (Å <sup>2</sup> )
L:TYR 49		7	C:ASN 430	8	L:SER 31		9	C:ASN 430	1
L:SER 56		5	C:SER 432	5	L:ASN 32		23	C:GLU 431	2
					L:TYR 49		22	C:LEU 433	115
					L:GLY 50		14	C:LYS 446	23
					LINK 53		1 21		
					LTYR 91		11		
Total		12	Total	13	Total		101	Total	141
					ļ				
HEPC3 hea	wy chain (H) and li	ght chain (L	) residues interacting w	vith E2core <sub>1a53</sub>	AR3C hea	avy chain (H) and I	ight chain (L)	residues interacting wit	1 E2core <sub>1a154</sub>
gly	ycans (chain C) (in	teractive par	rtners are grouped toge	ther)	g	glycans (chain C) (	interactive par	tners are grouped toget	her)
AD Chain	Bond	DOA (A )	E2COre <sub>1a53</sub> Bond	DOA (A)	AD Chain	Bond	10 DOA (A )	E2core <sub>1a154</sub> Bond	DOA (A )
L:1YR 49		27	C:NAG4301	56	LISER 30	ц	10	C:NAG 4301 H	101
LISER 56		16			L. TR 92	п	+∠ 28		
H:TYR 99		41	C:NAG4301	44	H:TYR 100		34	C:NAG 4301	44
H:SER 74		12	C:BMA6233	17	L:SER 30	н	20	C:NAG 4302 H	53
H:THR 75		4			L:TYR 92	н	35		
					L:ARG 93		2	0.000	0
1					L:GLN 27		3	C:MAN 4304	3
Total		114	Total	117	Total		174	Total	201

\* Type of putative interation: H - hydrogen bond, S - salt bridge. BSA: buried surface area, K. The AR3C-E2core<sub>154</sub> interface was previously reported to be dominated by V<sub>H</sub> domain (86% of the total BSA) and particularly CDRH3 loop (44% of the BSA) ( Kong et al., 2013)

Table S4: HEPC3 and HEPC74 interfaces with E2 ectodomains. Shared E2ecto contact residues, hydrogen bonds, and salt bridges are shaded grey. Related to Figure 2.

List of HE	PC3 heavy chain (c	hain H)-E2ect	to <sub>1b09</sub> (chain C) in	nterface r	esidues	List of H	EPC74 heavy chai	n (chain H)-E2e	cto <sub>1b09</sub> (chain C) ir	nterface	e residues
(the	residues on each r	ow are not ma	atched interactiv	ve partner	s)	(t	he residues on eac	h row are not n	natched interactive	e partn	ers)
Heavy chain	Bond	BSA (A <sup>-</sup> )	E2ecto <sub>1b09</sub>	Bond	BSA (A <sup>-</sup> )	Heavy chain	Bond	BSA (A <sup>-</sup> )	E2ecto <sub>1b09</sub>	Bond	BSA (A <sup>-</sup> )
H:GLN 1	н	47	C:ILE 414		16	H:GLY 26		3	C:TRP 420		1
HIGLY 20	ц	14	C:CLV 418	п	19		п ц	10	C:I EU 427	п	27 51
HIGET 27	н	73	C:SER /10	н	20	HITYR 20		138	C:ASN 428		1
H1 FU 29		76	C:TRP 420	н	5	H'II F 30	н	77	C:CYS 429	н	29
H:ASN 30	н	60	C:LEU 427		52	H:ASN 31		31	C:ASN 430		16
H:SER 31		5	C:ASN 428		10	H:TYR 32	н	16	C:ASP 431	н	35
H:GLU 33	н	10	C:CYS 429	н	34	H:ALA 33		3	C:SER 432		7
H:THR 52		9	C:ASN 430		19	H:PRO 52A		29	C:HIS 434	н	114
H:PRO 53	н	47	C:ASP 431	HS	40	H:ILE 53		47	C:THR 435	н	58
H:ILE 54		36	C:HIS 434	HS	90	H:SER 54		7	C:GLY 436		34
H:PHE 55		5	C:THR 435	н	33	H:ASN 55		49	C:PHE 437		13
H:GLU 56		2	C:GLY 436	н	30	H:ARG 94	н	24	C:LEU 438		57
H:GLU 73	S	16	C:PHE 437		1	H:LEU 96		46	C:ALA 439		38
H:ARG 94		24	C:LEU 438		48	H:LEU 97		73	C:ALA 440		16
H:GLY 96		3	C:ALA 439		42	H:LYS 98	Н	72	C:PHE 442		80
H:VAL 97		70	C:ALA 440		15	H:TYR 99		20	C:TYR 443		73
H:ARG 98	HS	83	C:LEU 441		1	H:CYS 100	н	68	C:HIS 445		54
H:TYR 99		31	C:PHE 442		37	H:GLY 100A	L .	7	C:LYS 446	н	59
H:CYS 100	н	77	C:TYR 443	н	98	H:GLY 100B	н	45	C:PHE 447		56
H:GLY 100A		9	C:HIS 445		2	H:GLY 1000	; н	69	C:ASN 448	н	63
H:GLY 100B		53	C:LYS 446	HS	133	H:ASN 100D	)	10	C:ALA 449		1
H:GLY 100C	н	86	C:PHE 447	н	27	H:CYS 100E		39	C:TRP 529	Н	32
H:ARG 100D	н	66	C:ASN 448	н	65	H:VAL 100J		11	C:GLU 531	н	45
H:CYS 100E		47	C:ALA 449		1	H:ASP 101	н	13	C:TRP 616		5
H:ASP 101	HS	26	C:TRP 529		26				C:PRO 619		6
H:PRO 102		5	C:GLU 531		29						
Tatal		090	<b>T</b> . ( . )		006	Tatal		0.07	<b>T</b> - 4 - 1		070
lotal		980	lotal		926	Iotal		987	lotal		972
	Hydroge	n bonds					Hydro	ogen bonds			
##	Heavy chain	Distance (Å)	E2ecto <sub>1b09</sub>			##	Heavy chain	Distance (Å)	E2ecto <sub>1b09</sub>		
1	H:GLY 100C[ O ]	2.9	C:TRP 420[ N	]		1	H:GLY 27[O]	3.0	C:ASN 448[ ND	2]	
2	H:CYS 100[ O ]	3.1	C:CYS 429[ N	]		2	H:THR 28[O]	2.9	C:ASN 448[ N	]	
3	H:ARG 98[ O ]	3.0	C:ASP 431[ N	]		3	H:LYS 98[O]	3.0	C:ASP 431[ N ]	]	
4	H:ASP 101[ OD2]	2.9	C:HIS 434[ NE	E2]		4	H:GLY 100B[ O ]	3.3	C:TRP 529[ NE	1]	
5	H:GLU 33[ OE1]	3.9	C:TYR 443[ C	)H ]		5	H:GLY 100C[ O ]	2.7	C:HIS 421[ NE2	2]	
6	H:PRO 53[O]	2.3	C:LYS 446[ N	Z ]		6	H:ASP 101[ O ]	3.8	C:HIS 434[ ND1	1]	
7	H:THR 28[O]	2.8	C:ASN 448[ N	]		7	H:CYS 100[ N ]	3.8	C:CYS 429[ O	]	
8	H:GLY 27[ O ]	2.9	C:ASN 448[ N	ID2]		8	H:ARG 94[NH1]	3.0	C:HIS 434[ O ]		
9	H:ARG 100D[ NH:	2.7	C:ASN 417[ C	)]		9	H:TYR 32[ OH ]	2.8	C:THR 435[ O	]	
10	H:ARG 100D[ NH	3.6	C:SER 419[ C	)G ]		10	H:ILE 30[N]	2.9	C:LYS 446[ O ]	]	
11	H:CYS 100[ N ]	2.9	C:CYS 429[ C	)]		11	H:GLY 100B[ N ]	2.2	C:GLU 531[ OE	[2]	
12	H:ARG 98[ NH1]	3.1	C:ASP 431[ O	D2]							
13	H:GLN 1[N]	3.9	C:HIS 434[ O	1							
14	H:THR 28[ OG1]	3.1	C:THR 435[ C	)]							
15	H:THR 28[ OG1]	3.7	C:GLY 436[ C	)]							
16	H:ASN 30[N]	2.9	C:LYS 446[ O	1							
17	H:ASN 30[ ND2]	3.4	C:PHE 447[ C	)]							
	Salt b	ridges									
##	Heavy chain	Distance (Å)	E2ecto <sub>1b09</sub>								
1	H:ASP 101[ OD2]	2.9	C:HIS 434[ NE	E2]							
2	H:GLU 73[ OE1]	3.8	C:LYS 446[ N	Z ]							
3	H:ARG 98[ NH1]	3.1	C:ASP 431[ O	D2]							
l ist of L	PC3 light chain (ch	nain I \-F?ect	Alen (chain C) in	terface ro	sidues	List of	HFPC74 light chair	(chain L)-F2or	to the (chain C) in	terfaco	residues
(the	residues on each r	ow are not m	atched interactiv	/e partner	s)	(†	he residues on eac	th row are not n	natched interactive	e partn	ers)
Light chain	Bond	BSA (Å <sup>2</sup> )	E2ecto <sub>1b09</sub>	Bond	ÉSA (Å <sup>2</sup> )	Light chain	Bond	BSA (Å <sup>2</sup> )	E2ecto <sub>1b09</sub>	Bond	BSA (Å <sup>2</sup> )
L:TYR 32	Н	29	C:GLY 418	Н	24	L:TYR 49		. /	C:ASN 430		14
L:TYR 49		15	C:ASN 430		16	L:GLU 55	HS	29	C:SER 432	н	32
L:GLN 55		16	C:SER 432		11	L:THR 56	н	48	C:LEU 433		9
L:SER 56		11	C:HIS 434		15				C:HIS 434	HS	33
Total		71	Total		65	Total		77	Total		88
	Hydroge	n bonds					Hydro	ogen bonds	<b>5</b> 0 ·		
##	Light chain	Distance (A)	E2ecto <sub>1b09</sub>			##	Light chain	Distance (A)	E2ecto <sub>1b09</sub>		
1	L:1YR 32[OH]	3.4	C:GLY 418[ C	)]			LIGLU 55[ OE1]	2.9	C:HIS 434[ NE2	<u>/</u> ]	
						∠ _	LITK 56[UG1]	3.1	U.SER 432[ U	1	
							Sal	t bridges			
						##	Heavy chain	Distance (Å)	E2ecto <sub>1b09</sub>		
						1	L:GLU 55[ OE1]	2.9	C:HIS 434[ NE2	2]	
						2	L:GLU 55[ OE2]	3.8	C:HIS 434[ NE2	2]	

HEPC3 heavy	chain (H) and	light chain (L) r	esidues interac	h E2ecto <sub>1b09</sub>	HEPC74 heavy chain (H) and light chain (L) residues interacting with E2ecto1b09						
glyca	ans (chain C) (	interactive partr	ners are groupe	d togeth	er)	glyd	cans (chain C)	(interactive parts	ners are grouped	togethe	r)
Ab chain	Bond	BSA (Å <sup>2</sup> )	E2ecto <sub>1b09</sub>	Bond	BSA (Å <sup>2</sup> )	Ab chain	Bond	BSA (Ų)	E2ecto <sub>1b09</sub>	Bond	BSA (Ų)
H:ALA 24		1	C:NAG4481	Н	153	H:GLN 1	Н	21	C:NAG4481	Н	178
H:SER 25		13				H:THR 24		7			
H:GLY 26	н	25				H:SER 25		17			
H:GLY 27	н	16				H:GLY 26	н	24			
H:LEU 29		8				H:GLY 27	н	18			
H:ASN 30		16				H:TYR 29		4			
H:TYR 32	н	3				H:ILE 30		26			
H:SER 76		12				H:SER 76		10			
L:TYR 49	н	28	C:NAG4301	н	84	L:TYR 49	н	25	C:NAG4301	н	79
L:ASN 53		24				L:LYS 50		10			
L:LEU 54		9				L:SER 53		14			
L:SER 56		20				L:LEU 54		6			
H:GLN 3		1	C:NAG4482	н	52	L:THR 56		11			
H:SER 25	н	19				H:LYS 98		2	C:NAG4301		16.99
H:GLY 26		26				H:TYR 99		15			
H:TYR 99		38	C:NAG4301		42	L:LEU 54		10	C:NAG4302		9
L:LEU 54		1	C:NAG4302	н	42						
L:SER 56	н	27									
L:GLY 57		7									
H:ARG 100D	н	31	C:NAG4171	н	31						
L:SER 60	н	29	C:BMA4303	н	24						
L:ASN 30		21	C:NAG4171		19						
Total		374	Total		447	Total		219	Total		283

\* Type of putative interation: H - hydrogen bond, S - salt bridge. BSA: buried surface area,  $\hat{\mathcal{K}}$ .

Table S5: Interface between HEPC46 and E2 proteins (E2ecto<sub>1a53</sub>, E2core<sub>1a53</sub>). Shared E2 contact residues, hydrogen bonds, and salt bridges are shaded grey. Related to Figure 2 and Figure S5.

List of HF	PC46 heavy chain	(chain A)-F2e	ctore (chain C)	interfac	e residues	List of H	FPC46 heavy chai	n (chain F)-F2c	ore (chain C) i	interface	residues
(the	e residues on each	row are not m	atched interactiv	ve partn	ers)	(th	e residues on eac	th row are not n	natched interactiv	ve partne	ers)
Heavy chain	Bond	BSA (Å <sup>2</sup> )	E2ecto <sub>1a53</sub>	Bond	BSA (Å <sup>2</sup> )	Heavy chain	Bond	BSA (Ų)	E2core <sub>1a53</sub>	Bond	BSA (Å <sup>2</sup> )
A:ILE 28		67	C:HIS 474		39	F:ILE 28		67	C:ILE 496		3
A:THR 30		12	C:ILE 496		4	F:THR 30		7	C:THR 510		7
A:SER 31	н	67	C:THR 510		8	F:SER 31	Н	63	C:VAL 514		12
A:HIS 32		14	C:VAL 514		17	F:HIS 32		24	C:ARG 521		7
A:GLY 33		14	C:VAL 538		21	F:GLY 33		14	C:VAL 538		24
A:TRP 50		29	C:ASN 540		45	F:TRP 50		20	C:ASN 540		36
A:ILE 51		4	C:ASN 541		8	F:ILE 51		4	C:ASN 541		5
A:SER 52	н	23	C:THR 542	н	66	F:SER 52	н	16	C:THR 542	н	74
A:TYR 53		95	C:ARG 543		29	F:TYR 53		94	C:ARG 543		39
A:ASN 54		34	C:PRO 544		4	F:ASN 54	н	32	C:PRO 544		8
A:TYR 56	н	84	C:PRO 545		58	F:TYR 56		65	C:PRO 545	н	77
		9	C1 EU 546	н	147	E-ALA 95		6	C1 EU 546		153
A:SER 96		28	C:CLV 547	н	21	F:SER 96		22	C:CLV 547	н	27
A:GLNL 07	ц	112	C:001 547		58	ECLN 07		80	CIGET J47		51
A.U.E. 00	11	65	C.ASN 546		10			05	C.ASN 546		31
AILE 98		65	C:TRP 549		19	FILE 98		95	C:TRP 549		22
			C:PRO 567		17				C:PRO 567		27
			C:SER 595	н	3				C:PRO 568		1
			C:ARG 596	н	9				C:CYS 569		4
			C:VAL 633		0				C:SER 595		9
			C:GLY 634	н	19				C:ARG 596		14
			C:VAL 636		24				C:GLY 634		15
			C:HIS 638		7				C:VAL 636		8
Total		657			622	Total		617	Total		630
	Hydroge	en bonds					Hydro	ogen bonds			
##	Heavy chain	Distance (A)	E2ecto <sub>1a53</sub>			##	Heavy chain	Distance (A)	E2core <sub>1a53</sub>		
1	A:SER 31[0]	3.3	C:THR 542[ N	N ]		1	F:SER 31[0]	3.2	C:THR 542[ N	1]	
2	A:SER 52[ OG ]	2.9	C:LEU 546[ C	) ]		2	F:SER 31[0]	2.8	C:THR 542[ C	)G1]	
3	A:SER 52[ OG ]	3.5	C:GLY 547[ C	D ]		3	F:SER 52[ OG ]	3.8	C:GLY 547[ C	)]	
4	A:TYR 56[ OH ]	3.8	C:GLY 634[ C	2 ]		4	F:ASN 54[ND2]	2.7	C:PRO 545[ C	01	
5	A:GLN 97[ NE2]	3.9	C:SER 595[ C	5 I					-	-	
6	A:GLN 97[ NE2]	3.1	C:ARG 596[ 0	01							
List of H	EPC46 light chain (	chain B)-E2ec	to <sub>1a53</sub> (chain C) i	nterface	residues	List of I	HEPC46 light chair	n (chain E)-E2co	ore <sub>1a53</sub> (chain C) ii	nterface	residues
List of H (the	EPC46 light chain ( e residues on each	chain B)-E2ec row are not m	to <sub>1a53</sub> (chain C) i natched interactio	nterface ve partn	e residues ers)	List of I	HEPC46 light chair ne residues on eac	n (chain E)-E2co h row are not n	ore <sub>1a53</sub> (chain C) in natched interactiv	nterface ve partne	residues ers)
List of H (the Light chain	EPC46 light chain ( e residues on each Bond	chain B)-E2ec row are not m BSA (Ų)	to <sub>1a53</sub> (chain C) in natched interaction E2ecto <sub>1a53</sub>	nterface ve partn Bond	e residues lers) BSA (A <sup>2</sup> )	List of I (th Light chain	HEPC46 light chair ne residues on eac Bond	n (chain E)-E2co h row are not n BSA (Å <sup>2</sup> )	pre <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub>	nterface ve partne Bond	residues ers) BSA (Å <sup>2</sup> )
List of H (the Light chain B:GLY 29	EPC46 light chain ( e residues on each Bond	chain B)-E2ec row are not m BSA (Å <sup>2</sup> ) 1	to <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470	nterface ve partn Bond	e residues ers) BSA (A <sup>z</sup> ) 1	List of I (th Light chain E:SER 30	HEPC46 light chair ne residues on eac Bond	n (chain E)-E2co h row are not n BSA (A <sup>2</sup> ) 15.7337	bre <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545	nterface ve partne Bond	residues ers) BSA (Å <sup>2</sup> ) 5.86376
List of H (the Light chain B:GLY 29 B:SER 30	EPC46 light chain ( e residues on each Bond	chain B)-E2ec row are not m BSA (A <sup>2</sup> ) 1 37	to <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471	nterface ve partn Bond	e residues ers) BSA (Å <sup>2</sup> ) 1 1	List of F (tr Light chain E:SER 30 E:ASN 31	HEPC46 light chair ne residues on eac Bond H	n (chain E)-E2co h row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429	cre <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546	nterface ve partne Bond	residues ers) BSA (Å <sup>2</sup> ) 5.86376 24.9079
List of H (the Light chain B:GLY 29 B:SER 30 B:ASN 31	EPC46 light chain (i e residues on each Bond H	chain B)-E2ec row are not m BSA (A <sup>2</sup> ) 1 37 16	to <sub>1a53</sub> (chain C) in hatched interaction E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472	nterface ve partn Bond	e residues ers) BSA (A <sup>2</sup> ) 1 1 1 2	List of F (tr Light chain E:SER 30 E:ASN 31 E:TYR 32	HEPC46 light chair ne residues on eac Bond H	n (chain E)-E2co h row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506	ore <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569	nterface ve partne Bond	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165
List of H (the Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32	EPC46 light chain (i e residues on each Bond H H	chain B)-E2ec row are not m BSA (A <sup>2</sup> ) 1 37 16 72	to <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473	nterface ve partn Bond	e residues ers) BSA (A <sup>2</sup> ) 1 1 12 9	List of I (tr Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53	HEPC46 light chair ne residues on eac Bond H	n (chain E)-E2cc h row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248	cret <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570	nterface ve partne Bond	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165 10.8951
List of H (thu Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51	EPC46 light chain (r e residues on each Bond H H H	chain B)-E2ec row are not m BSA (A <sup>2</sup> ) 1 37 16 72 1	to <sub>1a53</sub> (chain C) in natched interacti E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474	nterface ve partn Bond H	e residues ers) BSA (A <sup>2</sup> ) 1 1 12 9 29	List of I (tr Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91	HEPC46 light chair ne residues on eac Bond H	n (chain E)-E2cd th row are not n BSA (A <sup>4</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212	bre <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596	nterface ve partne Bond HS	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744
List of H (thu Eight chain B:GLY 29 B:SER 30 B:ASN 31 B:ASN 31 B:ASN 51 B:LYS 66	EPC46 light chain (i e residues on each Bond H H	chain B)-E2ec row are not m BSA (A <sup>2</sup> ) 1 37 16 72 1 1 1	tto <sub>1a53</sub> (chain C) in matched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546	nterface ve partn Bond H	residues ers) BSA (A <sup>2</sup> ) 1 1 1 12 9 29 28	List of H (tr Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93	HEPC46 light chair he residues on eac Bond H H	n (chain E)-E2cd h row are not n BSA (A <sup>4</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637	cre <sub>ta53</sub> (chain C) ii natched interactiv E2core <sub>ta53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597	nterface ve partne Bond HS	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859
List of H (the Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91	EPC46 light chain ( e residues on each Bond H H	chain B)-E2ec row are not m BSA (A <sup>2</sup> ) 1 37 16 72 1 1 28	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591	nterface ve partn Bond H	residues ers) BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35	List of I (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93	HEPC46 light chair ne residues on eac Bond H HS	n (chain E)-E2cd th row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637	cre <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597	nterface ve partne Bond HS	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859
List of H (thu Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93	EPC46 light chain (v e residues on each Bond H H H	chain B)-E2ec row are not m BSA (A <sup>4</sup> ) 1 37 16 72 1 1 1 28 21	tto <sub>1a53</sub> (chain C) in natched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596	nterface ve partn Bond H	residues ers) BSA (A <sup>2</sup> ) 1 1 1 2 9 29 28 35 52	List of I (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93	HEPC46 light chair ne residues on eac Bond H HS	n (chain E)-E2ca h row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637	c:PRO 545 C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597	nterface ve partne Bond HS	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93	EPC46 light chain (r e residues on each Bond H H H	chain B)-E2ec row are not m BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21	to <sub>1a53</sub> (chain C) in atched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596	nterface ve partn Bond H HS	residues BSA (Å <sup>2</sup> ) 1 1 1 2 9 29 28 35 52	List of I (tt Light chain E:SER 30 E:ASN 31 E:TRY 32 E:GLN 53 E:TRP 91 E:ASP 93	HEPC46 light chair ne residues on eac Bond H HS	n (chain E)-E2ca h row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637	c:PRO 545 C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597	nterface ve partne Bond HS	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859
List of H (th) B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total	EPC46 light chain (r e residues on each Bond H H H	chain B)-E2ec row are not m BSA (A <sup>c</sup> ) 1 37 16 72 1 1 1 28 21 21 177	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:CLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total	nterface ve partn Bond H HS	residues ers) BSA (A <sup>2</sup> ) 1 1 1 2 9 29 28 35 52 52 168	List of f (tr Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total	HEPC46 light chair ne residues on eac Bond H HS	a (chain E)-E2cc th row are not in BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138	Total	nterface ve partne Bond HS	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total	EPC46 light chain (r e residues on each Bond H H H	chain B)-E2ec row are not m BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 28 21	tto <sub>1a55</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:ILE 546 C:GLU 591 C:ARG 596 Total	nterface ve partn Bond H HS	residues BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total	HEPC46 light chair ne residues on eac Bond H H	(chain E)-E2cc th row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138	Total	nterface ye partne Bond HS	residues ers) BSA (A <sup>*</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total	EPC46 light chain ( e residues on each Bond H H H HS	chain B)-E2ec row are not m BSA (Å <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 27 20 bonds	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1853</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total	nterface ve partn Bond H HS	Presidues BSA (Å <sup>2</sup> ) 1 1 12 9 29 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:SER 30 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total	HEPC46 light chair te residues on eac Bond H HS HS	(chain E)-E2cd th row are not n BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 138 ogen bonds	tore <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total	nterface ve partne Bond HS	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ##	EPC46 light chain ( e residues on each Bond H H HS HS	chain B)-E2ec row are not m BSA (A <sup>c</sup> ) 1 3 7 16 72 1 1 28 21 1 28 21 177 28 21 177 28 21 177 28 21	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub>	nterface ve partn Bond H HS	residues BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 52 168	List of I (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total	HEPC46 light chair ne residues on eac Bond H HS HS	n (chain E)-E2cd ch row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 20gen bonds Distance (Å)	C:PRO 545 C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total	HS	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[ OD1]	chain B)-E2ec row are not m BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 1 28 21 177 27 20 177 28 21 177 29 1000ds Distance (Å) 3.8	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596 [N	nterface ve partn Bond H HS	residues ers) BSA (A <sup>4</sup> ) 1 1 1 2 9 29 28 35 52 52 168	List of I (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1	HEPC46 light chair ne residues on eac Bond H HS HS Light chain E:ASN 31[ OD1]	a (chain E)-E2ca th row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (A) 2.6	Dre <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N	HS	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2	EPC46 light chain ( <u>e residues on each</u> Bond H H HS HS <u>Hydroge</u> Light chain B:ASN 31[OD1] B:TVR 32[OH]	chain B)-E2ec row are not n BSA (A <sup>c</sup> ) 1 37 16 72 1 1 1 28 21 177 28 21 177 <b>en bonds</b> Distance (Å) 3.8 3.4	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:CLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:ARG 596] N C:ARG 596[ N	nterface ve partn Bond H HS NH2]	residues BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chair te residues on eac Bond H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2]	a (chain E)-E2cc ch row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6	Total E2core <sub>1a53</sub> (chain C) in E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N	HS HS	residues ers) BSA (A <sup>*</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3	EPC46 light chain ( e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH]	chain B)-E2ec row are not m BSA (Å <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 28 21 1777 en bonds Distance (Å) 3.8 3.4 2.7	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:HIS 474[ N	H H HS NH2] D1]	residues ers) BSA (Å <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of I (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chain ne residues on eac Bond H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2]	a (chain E)-E2cd th row are not n BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 ogen bonds Distance (Å) 2.6 2.5	C:ARG 596[ N C:ARG 596 N C:ARG 596 N C:CYS 589 C:ALA 570 C:ARG 596 C:CYS 597	HEPFACE ve partne Bond HS HS H2]	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:TYR 32[OH]	chain B)-E2ec row are not rr BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 1 177 28 21 177 27 50 50 50 50 50 50 50 50 50 50 50 50 50	tto1a53 (chain C) in hatched interactiv E2ecto1a53 C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto1a53 C:ARG 596[ N C:HIS 474[ N C:HIS 474[ N	nterface ve partn Bond H HS NH2] ] D1] NH2]	residues ers) BSA (A <sup>4</sup> ) 1 1 2 9 29 28 35 52 52 168	List of I (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chair ne residues on eac Bond H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2]	a (chain E)-E2ca th row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5	Total E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N	HS H2] H2]	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5	EPC46 light chain ( e residues on each Bond H H HS HS Light chain B:ASN 31[ OD1] B:TYR 32[ OH ] B:ASP 93[ OD1] B:ASP 93[ OD1]	chain B)-E2ec row are not r BSA (A <sup>2</sup> ) 1 37 16 72 1 1 28 21 177 28 21 177 28 21 177 28 21 3.8 3.4 2.7 3.5 3.3	tto <sub>1a53</sub> (chain C) in hatched interactif E2ecto <sub>1a53</sub> C:CLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:HIS 474[ N C:HIS 474[ N C:ARG 596[ N	NH2] NH2] NH2] NH2]	residues BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chair ne residues on eac Bond H HS HS Light chain E:ASP 93[ OD2]	a (chain E)-E2cc th row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5	Total E2core1a53 C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core1a53 C:ARG 596[ N C:ARG 596[ N	HS H2]	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5	EPC46 light chain ( e residues on each Bond H H HS HS Hydroge Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2]	chain B)-E2ec row are not n BSA (A <sup>c</sup> ) 1 37 16 72 1 1 1 28 21 177 28 21 177 28 21 177 28 21 3.4 2.1 3.4 2.7 3.5 3.3	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:HIS 474[ N C:ARG 596[ N C:ARG 596[ N	nterface ve partn Bond H HS HS NH2] D1] NH2] NH2]	residues ers) BSA (A <sup>2</sup> ) 1 12 9 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chain te residues on eac Bond H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2]	a (chain E)-E2cc ch row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 <b>Distance</b> (Å) 2.6 2.5	Total E2core <sub>1a53</sub> (chain C) in E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N	HS HS	residues ers) BSA (A <sup>*</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5	EPC46 light chain ( e residues on each Bond H H HS HS Hydroge Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt b Salt b	chain B)-E2ec row are not m BSA (A <sup>r</sup> ) 1 37 16 72 1 1 1 28 21 177 28 21 177 28 21 177 28 21 3.8 3.8 3.8 3.8 3.4 2.7 3.5 3.3 3.9	to1a53 (chain C) in hatched interactiv E2ecto1a53 C:GLY 470 C:PR0 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto1a53 C:ARG 596[ N C:HIS 474[ N C:HIS 474[ N C:ARG 596[ N	NH2] NH2] NH2] NH2]	residues ers) BSA (Å <sup>2</sup> ) 1 12 9 29 29 28 35 52 168	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chair te residues on eac Bond H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2]	(chain E)-E2cc th row are not n BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 <b>ogen bonds</b> Distance (A) 2.6 2.5 t bridges	E2core <sub>1a53</sub> (chain C) in natched interactiv E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N	Nterface ye partne Bond HS HS	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5 	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt L Light chain	chain B)-E2ec row are not m BSA (Å <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 en bonds Distance (Å) 3.8 3.4 2.7 3.5 3.3 wridges Distance (Å)	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:HIS 474[ N C:ARG 596[ N C:ARG 596[ N	NH2] D1] NH2] NH2]	residues ers) BSA (Å <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chain ne residues on eac Bond H HS HS Light chain E:ASN 31[OD1] E:ASP 93[OD2] Sal Light chain	a (chain E)-E2cd th row are not n BSA (A <sup>2</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5 t bridges Distance (Å)	C:ARG 596[ N C:ARG 596[ N C:ARG 596] C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597	HS H2]	residues ers) BSA (A <sup>4</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5 	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt E Light chain B:ASP 93[OD1]	chain B)-E2ec row are not rr BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 28 21 177 27 20 50 50 3.8 3.4 2.7 3.5 3.3 17 10 50 50 3.5 3.5 3.5	to1a53 (chain C) in hatched interactiv E2ecto1a53 C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto1a53 C:ARG 596 N C:ARG 596 N C:ARG 596 N C:ARG 596 N	NH2] NH2] NH2] NH2] NH2]	residues ers) BSA (A <sup>4</sup> ) 1 1 12 9 29 28 35 52 52 168	List of R (tt) Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2	HEPC46 light chair ne residues on eac Bond H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2]	a (chain E)-E2cc th row are not in BSA (Å') 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5 t bridges Distance (Å) 3.1	cre1:s53 (chain C) in natched interactive E2core1:s53   C:PRO 545 C:LEU 546   C:CYS 569 C:ALA 570   C:ARG 596 C:CYS 597   Total   E2core1:s53   C:ARG 596[ N C:ARG 596[ N   C:ARG 596[ N C:ARG 596[ N   C:ARG 596[ N C:ARG 596[ N	HS HS H2] H2]	residues ers) 5.863 (A <sup>*</sup> ) 5.48079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ### 1 2 3 4 5 	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt t Light chain B:ASP 93[OD1] B:ASP 93[OD2]	chain B)-E2ec row are not rr BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 28 21 177 28 21 177 28 21 3.8 3.4 2.7 3.8 3.4 2.7 3.5 3.3 7 10 10 10 10 10 10 10 10 10 10 10 10 10	to1a53 (chain C) in hatched interactiv E2ecto1a53 C:CLY 470 C:PR0 471 C:ILE 472 C:SER 473 C:ILE 472 C:SER 473 C:ILE 546 C:GLU 591 C:ARG 596 Total E2ecto1a53 C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N	NH2] NH2] NH2] NH2] NH2] NH2]	residues BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2	HEPC46 light chain ne residues on eac Bond H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2]	a (chain E)-E2cc th row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5 t bridges Distance (Å) 3.1 2.5	Dret_1853 (chain C) in natched interactive E2core11853   C:PRO 5454 C:LEU 546   C:CYS 569 C:ALA 570   C:ARG 596 C:CYS 597   Total   E2core11853   C:ARG 596[ N C:ARG 596[ N   C:ARG 596[ N C:ARG 596[ N   E2core11853   C:ARG 596[ N C:ARG 596[ N   C:ARG 596[ N   C:ARG 596[ N   C:ARG 596[ N   C:ARG 596[ N   C:ARG 596[ N	HS H2] H2] H2] H2]	residues ers) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5 ## 1 2	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt L Light chain B:ASP 93[OD2]	chain B)-E2ec row are not r BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 28 21 177 28 21 177 28 21 3.8 3.4 2.7 3.8 3.4 2.7 3.5 3.3 20 10 10 10 10 10 10 10 10 10 10 10 10 10	to 1.853 (chain C) in hatched interactif E2ecto 1.853 C:CLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:ILE 546 C:GLU 591 C:ARG 596 Total E2ecto 1.853 C:ARG 596 N C:ARG 596 E2ecto 1.853 C:ARG 596 C:ARG 596 C:AR	NH2] NH2] NH2] NH2] NH2] NH2] NH2]	residues ers) BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2	HEPC46 light chair ne residues on eac Bond H H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD1] E:ASP 93[ OD2]	a (chain E)-E2cc th row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.5 t bridges Distance (Å) 3.1 2.5	E2core1a63 C:PRO 545 C:LEU 546 C:CLEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core1a63 C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N	HS HS H2] H2] H2] H2]	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:ASN 31 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5 5 # ## 1 2 2 3 4 5	EPC46 light chain ( e residues on each Bond H H HS HS HS HS HS HS HS HS	chain B)-E2ec row are not r BSA (A <sup>2</sup> ) 1 37 16 72 1 1 28 21 177 28 21 177 28 21 177 28 21 3.3 3.4 2.7 3.3 3.4 2.7 3.5 3.3 7 Distance (Å) 3.5 3.3 7 Distance (Å) 3.5 3.3 7 Distance (Å) 3.5 3.3	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:CLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:ILE 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596 N C:HIS 474 N C:HIS 474 N C:HIS 474 N C:ARG 596 C:ARG 596 C:ARG 596 C:ARG 596 C:ARG 596 C:ARG 596 N C:ARG 596 C:ARG 596	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	n residues ers) BSA (A <sup>2</sup> ) 1 12 9 29 28 35 52 168	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h	HEPC46 light chair ne residues on eac Bond H H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] E:ASP 93[ OD2] E:ASP 93[ OD2]	(chain E)-E2cc th row are not n BSA (Å <sup>-</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5 t bridges Distance (Å) 3.1 2.5	Total E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CLEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[	HS H2 H2 H2 H2 H2 H2 H2 H2 H2 H2 H2 H2 H2	residues ers) BSA (A <sup>+</sup> ) 5.66376 24.9079 25.165 10.8951 87.1744 1.15859 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5 5 	EPC46 light chain ( e residues on each Bond H H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Satt E Light chain B:ASP 93[OD2] Satt b Light chain B:ASP 93[OD2] avy chain (A) and li ycans (chain C) (int)	chain B)-E2ec row are not m BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 28 21 177 28 21 177 28 21 3.3 21 0istance (A) 3.8 3.4 2.7 3.5 3.3 0istance (A) 3.3 0istance (A) 3.3 0istance (A) 3.3	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:HIS 474[ N C:HIS 474[ N C:ARG 596[ N	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	h E2ecto <sub>1a53</sub>	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h	HEPC46 light chair residues on eac Bond H H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] E:ASP 93[ OD2] E:ASP 93[ OD2] E:ASP 93[ OD2]	(chain E)-E2cc th row are not n BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5 t bridges Distance (Å) 3.1 2.5 t bridges Distance (Å) 3.1 2.5	E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N C:ARG 596 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N	HS HS HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total 70tal 4 5 4 5 4 5 4 5 4 5 4 5 4 5	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt b Light chain B:ASP 93[OD2] Salt b Light chain B:ASP 93[OD2] avy chain (A) and li ycans (chain C) (int	chain B)-E2ec row are not m BSA (A <sup>*</sup> ) 1 37 16 72 1 1 28 21 177 en bonds Distance (A) 3.8 3.4 2.7 3.5 3.3 Distance (A) 3.5 3.3 Distance (A) 3.5 3.3 Distance (A) 3.5 3.3	tto <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:ILE 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:HIS 474[ N C:HIS 474[ N C:HIS 474[ N C:ARG 596] N E2ecto <sub>1a53</sub> C:ARG 596[ N E2ecto <sub>1a53</sub>	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	h E2ecto <sub>1a53</sub> er) BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h S Ab chain	HEPC46 light chair te residues on eac Bond H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] E:ASP 93[ OD2] eavy chain (F) anc Jlycans (chain C) (	t ichain E)-E2cd h row are not n BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (A) 2.6 2.5 t bridges Distance (A) 3.1 2.5 t bridges Distance (A) 3.1 2.5	E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596] C:ARG 596 C:CYS 597 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596] N	HS HS HS HS H2] H2] H2] H2] H2] H2] H2] H2] H2] H2]	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155 155 155 <b>155</b>
List of H (th) Eight chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total 70tal 1 2 3 4 5 5 4 5 5 4 5 5 4 5 5 4 5 5 7 7 1 2 2 7 7 1 2 2 7 7 1 2 2 7 7 7 7 7	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Sait E Light chain B:ASP 93[OD1] B:ASP 93[OD1] B:ASP 93[OD2] avy chain (A) and li ycans (chain C) (int	chain B)-E2ec row are not rr BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 en bonds Distance (Å) 3.8 3.4 2.7 3.5 3.3 Distance (Å) 3.5 3.5 3.3 Distance (Å) 3.5 3.3 Distance (Å) Bistance (Å)	tto1a53 (chain C) in hatched interactiv E2ecto1a53 C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto1a53 C:ARG 596[ N C:ARG 596[ N] C:ARG 596[ N C:ARG 596[ N] C C:ARG 596[ N] C C C:ARG 596[ N] C C C C C C C C C C C C C C	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	residues   BSA (Ų)   1   1   12   9   29   28   35   52   168   h E2ecto1a53   er)   BSA (Ų)   81	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h CAb chain F:GLY 26	HEPC46 light chair ne residues on eac Bond H H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] eavy chain (F) and Jycans (chain C) ( Bond	(chain E)-E2cc h row are not n BSA (Å') 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (Å) 2.6 2.5 t bridges Distance (Å) 3.1 2.5 t bridges Iight chain (E) interactive part BSA (A') 4	E2core1a53 C:ARG 596[ N C:ARG 5965 C:LEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core1a53 C:ARG 596[ N C:ARG 596[ N	HS HS HS HS HS HZ] HZ] HZ] HZ] HZ] HZ] HZ] HZ] HZ] HZ]	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155 155 155 155 155 155 155 1
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total ## 1 2 3 4 5 ## 1 2 3 4 5 ## 1 2 2 3 4 5 ## 2 4 5 ## 2 4 5 ## 2 4 5 ## 2 4 4 5 ## 4 5 ## 4 5 ## 4 2 2 ## 4 2 2 ## 4 4 5 ## 4 4 5 ## 4 4 4 5 ## 4 4 4 4	EPC46 light chain (r e residues on each Bond H H H HS US EXENTION B:ASN 31[OD1] B:ASN 31[OD1] B:TYR 32[OH] B:ASP 93[OD1] B:ASP 93[OD2] Salt L Light chain B:ASP 93[OD2] Salt b Light chain B:ASP 93[OD2] Salt b Light chain B:ASP 93[OD2] Salt b Light chain B:ASP 93[OD2] Salt b C Light chain B:ASP 93[OD2] Salt b C C C C C C C C C C C C C C C C C C C	chain B)-E2ec row are not r BSA (A <sup>2</sup> ) 1 37 16 72 1 1 28 21 177 en bonds Distance (Å) 3.8 3.4 2.7 3.8 3.4 2.7 3.3 Distance (Å) 3.5 3.3 Distance (Å) 3.5 3.3 Distance (Å) 3.5 3.3	to1a53 (chain C) in hatched interactiv E2ecto1a53 C:CLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:ILE 546 C:GLU 591 C:ARG 596 Total E2ecto1a53 C:ARG 596[ N C:HIS 474[ N C:HIS 474[ N C:ARG 596[ N]	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	h residues BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168 h E2ecto <sub>1a53</sub> er) BSA (A <sup>*</sup> ) 81	List of f (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h G Ab chain F:GLY 26 F:TYR 27	HEPC46 light chair ne residues on eac Bond H H HS HS Light chain E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] E:ASP 93[ OD2] E:ASP 93[ OD2] E:ASP 93[ OD2] E:ASP 93[ OD2]	Ichain E)-E2cc   th row are not in   BSA (Å')   15.7337   19.9429   43.6506   10.3248   31.212   16.9637   138   Distance (Å)   2.6   2.5   Ibistance (Å)   3.1   2.5   Ilight chain (E)   interactive part   BSA (A')   4   16	C:ARG 596[ N C:ARG 596[ N C:ARG 596] C:ARG 596 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total C:ARG 596 C:CYS 597 Total C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596] N C:A	HS HS HS HS HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ HZ	residues ers) BSA (A <sup>+</sup> ) 5.66376 24.9079 25.165 10.8951 87.1744 1.15859 155 155
List of H (th) Light chain B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total 7 total 7 total 7 4 5 5 HEPC46 he g Ab chain A:GLY 26 A:TYR 27 A:LE 28	EPC46 light chain ( e residues on each Bond H H H HS HS Hydrogy Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Salt b Light chain B:ASP 93[OD1] B:ASP	chain B)-E2ec row are not n BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 en bonds Distance (A) 3.8 3.4 2.7 3.5 3.3 Distance (A) 3.5 3.3 Distance (A) 3.5 3.3 Distance (A) 3.5 3.3 Distance (A) 3.5 3.3	to <sub>1a53</sub> (chain C) in hatched interactiv E2ecto <sub>1a53</sub> C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:ILE 546 C:GLU 591 C:ARG 596 Total E2ecto <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N E2ecto <sub>1a53</sub> C:ARG 596] N	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	h E2ecto <sub>1453</sub> BSA (A <sup>2</sup> ) 1 1 12 9 29 28 35 52 168 h E2ecto <sub>1453</sub> er) BSA (A <sup>2</sup> ) 81	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h Schain F:GLY 26 F:TYR 27 F:ILE 28	HEPC46 light chain te residues on eac Bond H H HS HS Light chain E:ASN 31[ OD1] E:ASP 93[ OD2] Sal Light chain E:ASP 93[ OD2] E:ASP 93[ OD2] eavy chain (F) and Jycans (chain C) (	(chain E)-E2cc th row are not m BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (A) 2.6 2.5 t bridges Distance (A) 3.1 2.5 t bridges Distance (A) 3.7 C	E2core <sub>1a53</sub> C:PRO 545 C:LEU 546 C:CLEU 546 C:CYS 569 C:ALA 570 C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596] N	HS HS HS HS HZ] HZ] HZ] HZ] HZ] HZ] HZ] HZ] HZ] HZ]	residues ers) BSA (A <sup>+</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155 155
List of H (th) B:GLY 29 B:SER 30 B:ASN 31 B:TYR 32 B:ASN 51 B:LYS 66 B:TRP 91 B:ASP 93 Total 70tal 4 1 2 3 4 4 5 	EPC46 light chain (r e residues on each Bond H H HS HS Light chain B:ASN 31[OD1] B:TYR 32[OH] B:TYR 32[OH] B:TYR 32[OH] B:ASP 93[OD2] Sait b Light chain B:ASP 93[OD2] Sait b Light chain B:ASP 93[OD2] avy chain (A) and li ycans (chain C) (int Bond	chain B)-E2ec row are not rr BSA (A <sup>c</sup> ) 1 37 16 72 1 1 28 21 177 en bonds Distance (A) 3.8 3.4 2.7 3.5 3.3 Vridges Distance (A) 3.5 3.3 Vridges Distance (A) 8 Vridges Distance (A) 8 Vrid 8 Vridges Di	tto 1.a53 (chain C) in hatched interactiv E2ecto 1.a53 C:GLY 470 C:PRO 471 C:ILE 472 C:SER 473 C:HIS 474 C:LEU 546 C:GLU 591 C:ARG 596 Total E2ecto 1.a53 C:ARG 596[ N C:ARG 596[ N] (C C:ARG 596[	NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2] NH2]	Presidues   BSA (Ų)   1   1   12   9   29   28   35   52   168	List of H (tt Light chain E:SER 30 E:ASN 31 E:TYR 32 E:GLN 53 E:TRP 91 E:ASP 93 Total ## 1 2 ## 1 2 HEPC46 h S Chain F:GLY 26 F:TYR 27 F:ILE 28	HEPC46 light chain te residues on eac Bond H HS HS Light chain E:ASN 31[OD1] E:ASP 93[OD2] Sal Light chain E:ASP 93[OD2] E:ASP 93[OD2] eavy chain (F) anc plycans (chain C) ( Bond H	a (chain E)-E2cc th row are not n BSA (A <sup>c</sup> ) 15.7337 19.9429 43.6506 10.3248 31.212 16.9637 138 Distance (A) 2.6 2.5 t bridges Distance (A) 3.1 2.5 t bridges BSA (A <sup>c</sup> ) A A BSA (A <sup>c</sup> )	C:ARG 596[ N C:ARG 596[ N C:ARG 596] N C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596 C:CYS 597 Total E2core <sub>1a53</sub> C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596[ N C:ARG 596] N C:ARG 596[ N C:ARG 596] N	HS HS HS HS H2] H2] H2] H2] H2] H2] H2] H2] H2] H2]	residues ers) BSA (A <sup>2</sup> ) 5.86376 24.9079 25.165 10.8951 87.1744 1.15859 155 155 155

81

Total

57

Total

73

\* Type of putative interation: H - hydrogen bond, S - salt bridge. BSA: buried surface area,  $\hat{\mathcal{K}}$ .

Total

70

Total