

## Supplementary Materials for

### **Characterization of a vaccine-elicited human antibody with sequence homology to VRC01-class antibodies that binds the C1C2 gp120 domain**

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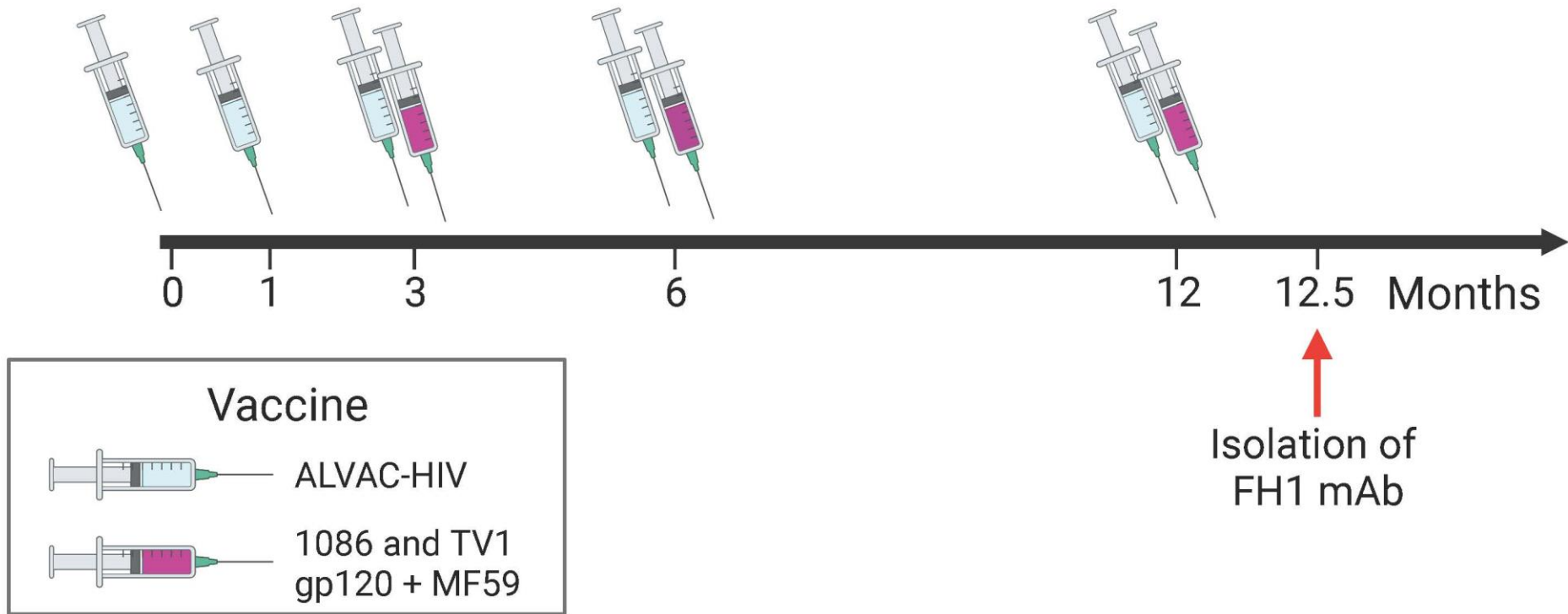
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**Figure S1**

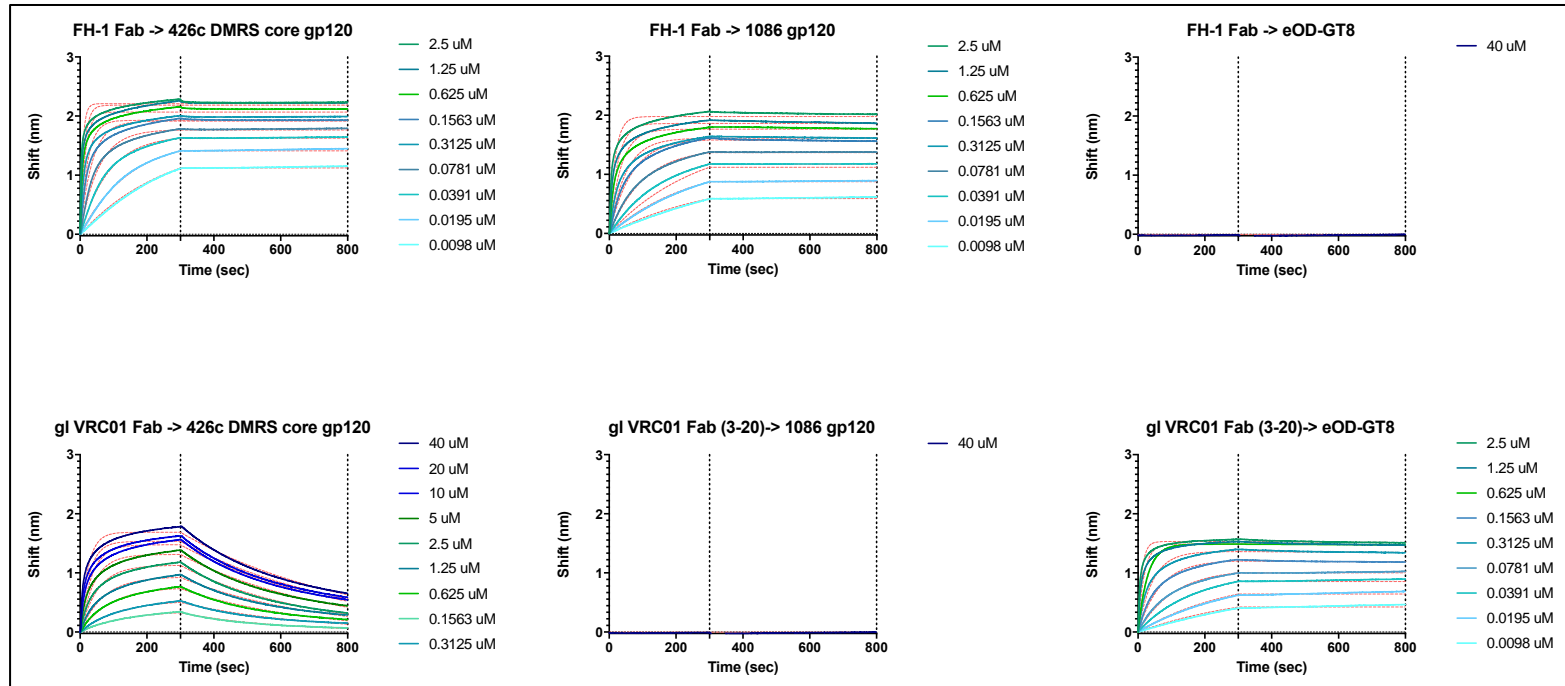
## HVTN 100 Clinical Trial



**S1. Timeline of vaccine administration in HVTN 100.** Numbers along the timeline indicate months since enrollment. Blue syringes denote administration of ALVAC, while red syringes denote administration of the bivalent rec gp120 mix (1086 and TV1). The red arrow indicates the visit (2 weeks post-5<sup>th</sup> immunization at visit 12) during which Env+ BCR repertoire analysis was performed and FH1 was isolated.

**Figure S2**

		KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	Full R <sup>2</sup>
FH-1 Fab	DMRScore gp120	2.64E-09	8.62E-11	2.43E+05	2.01E+03	2.79E-05	4.64E-06	0.9865
	1086 gp120	2.14E-10	2.71E-11	1.63E+05	2.23E+03	2.06E-05	3.05E-06	0.9904
	eOD-GT8	-	-	-	-	-	-	-
gl VRC01 Fab (3-20)	DMRScore gp120	6.09E-07	9.44E-09	9.67E+03	1.50E+02	2.48E-03	1.13E-05	0.9878
	1086 gp120	-	-	-	-	-	-	-
	eOD-GT8	1.67E-09	5.48E-11	1.44E+05	1.51E+03	1.57E-04	4.04E-06	0.9715



**S2. Kinetic analysis.** Kinetic analyses were performed by BLI using recombinant Fabs loaded onto FAB2G biosensors and 2-fold dilutions of the indicated Env monomers.

Supplementary Table 1 | Data collection and refinement statistics for FH1Fab+HXb2core

FH1Fab+HXb2core	
<b>Data collection</b>	
Space group	P1
Cell dimensions	
a, b, c (Å)	103.361, 106.266, 113.219
$\alpha$ , $\beta$ , $\gamma$ (°)	67.566, 76.674, 60.987
Resolution (Å)	50 - 3.5 (3.56 - 3.50)*
$R_{\text{sym}}$ or $R_{\text{merge}}$	0.120 (0.511)*
$I/\sigma I$	5.29 (1.19)*
Completeness (%)	92.5 (69.3)*
Redundancy	1.6 (1.4)*
$CC_{1/2}$	0.950 (0.712)*
<b>Refinement</b>	
Resolution (Å)	50.13 - 3.547 (3.674 - 3.547)*
No. reflections	36171 (888)
$R_{\text{work}}/R_{\text{free}}$	25.64/29.27 (28.32/30.22)*
No. atoms	22151
Protein	21280
Water	104
Ligand	767
B-factors (Å <sup>2</sup> )	78.88
Protein	78.55
Water	36.57
Ligand	93.73
R.m.s deviations	
Bond lengths (Å)	0.009
Bond angles (°)	1.29
Ramachdran Favored %	94.39
Ramachdran Outliers %	0.00
MolProbity all-atoms clashscore	6.49
<b>PDB ID</b>	

\* Statistics for the highest-resolution shell are shown in parentheses.

Supplementary Table 2 | Detailed interactions between FH1 and HXB2core (from Pisa web server, www.ebi.ac.uk).

a. Detailed interactions of HXB2core and FH1 Heavy Chain.

HXB2core	HSDC	ASA	BSA	FH1 Heavy Chain	HSDC	ASA	BSA
D:THR 51		104.27	1.73	U:THR 30		46.24	1.48
D:PHE 53		93.83	57.70	U:GLY 31		54.92	38.35
D:ALA 55		1.17	1.01	U:TYR 33	H	48.48	41.62
D:ASP 57		103.06	6.85	U:TRP 47		84.18	10.33
D:ALA 58	H	27.63	14.84	U:TRP 50		42.68	19.83
D:LYS 59		107.62	4.52	U:ASN 52		25.35	17.79
D:ALA 60	H	89.46	65.57	U:ASN 53	H	106.21	31.12
D:TYR 61	H	166.38	130.38	U:ASP 56		89.44	6.75
D:ASP 62		55.32	2.25	U:THR 57		47.77	8.83
D:THR 63		118.64	17.66	U:ASN 58	H	63.67	53.72
D:VAL 68		79.57	8.54	U:TYR 59	H	51.02	29.81
D:THR 71		44.03	1.67	U:ALA 60		21.99	4.43
D:VAL 75		85.76	58.89	U:GLN 61		178.08	66.44
D:PRO 76		97.65	74.49	U:GLN 64		120.29	35.01
D:THR 77	H	46.10	13.53	U:TRP 95		20.75	19.38
D:ASP 78		77.94	31.26	U:TRP 97		187.86	144.66
D:PRO 79		128.97	109.06	U:GLY 98		34.47	6.05
D:ASN 80	H	109.70	33.69	U:GLN 99	H	165.23	109.64
D:CYS 218		10.95	8.63	U:TRP 100A		141.06	16.79
D:PRO 220		19.47	11.94				
D:ALA 221	H	98.06	24.52				
D:GLN 246		87.28	11.78				

Hydrogen Bonds		
HXB2core	Dist. [Å]	FH1 Heavy Chain
D:ALA 60[N ]	3.27	U:ASN 58[ OD1]
D:TYR 61[N ]	3.33	U:TYR 59[ O ]
D:ALA 221[N ]	3.02	U:GLN 99[ OE1]
D:THR 77[ O ]	2.80	U:TYR 33[ OH ]
D:ASN 80[ OD1]	3.66	U:ASN 53[ ND2]
D:ALA 58[ O ]	2.88	U:ASN 58[ ND2]

b. Detailed interactions of HXB2core and FH1 Light Chain.

HXB2core	HSDC	ASA	BSA	FH1 Light Chain	HSDC	ASA	BSA
D:THR 51		104.27	9.54	V:GLU 1		147.36	11.74
D:PHE 53		93.83	11.30	V:ILE 2		49.88	33.80
D:CYS 54		2.98	0.12	V:GLN 27	H	109.42	53.81
D:ALA 58		27.63	1.11	V:SER 27A		75.42	2.21
D:ALA 60		89.46	15.90	V:VAL 28		13.44	1.00
D:VAL 68		79.57	8.61	V:ARG 29	HS	178.28	70.04
D:THR 71		44.03	34.91	V:TYR 32		117.06	76.44
D:HIS 72		165.12	130.61	V:HIS 90		20.68	20.37
D:ALA 73		49.92	35.41	V:MET 91		91.78	51.06
D:CYS 74		28.91	19.26	V:TYR 96		183.71	74.32
D:VAL 75		85.76	26.88	V:THR 97		42.63	10.16
D:PRO 76		97.65	23.16				
D:GLU 106		110.31	1.47				
D:ASP 107	HS	39.23	21.32				
D:SER 110		51.85	7.10				
D:GLN 114	H	108.60	51.50				

Hydrogen Bonds		
HXB2core	Dist. [Å]	FH1 Light Chain
D:GLN 114[ NE2]	2.64	V:GLN 27[ OE1]
D:ASP 107[ OD1]	3.50	V:ARG 29[ NH2]

Salt Bridges		
HXB2core	Dist. [Å]	FH1 Light Chain
D:ASP 107[ OD1]	3.50	V:ARG 29[ NH2]