Supplementary Information for

Quantifying the contribution of Fc-mediated effector functions to the antiviral activity of anti-HIV-1 IgG1 antibodies *in vivo*

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$$\frac{dT^*}{dt} = kVT - \delta T^* \quad (1)$$

$$\frac{dV}{dt} = N\delta T^* - cV \quad (2)$$

Fig. S1. Mathematical equations describing the dynamics of productively HIV-1-infected CD4 T cells (T*) and plasma virus particles (V). T, uninfected but susceptible CD4 T cells; k, infectivity constant of virions for susceptible CD4 T cells; δ, the death rate of productively infected CD4 T cells; c, HIV particle clearance rate; and N, the burst size or the number of virions produced by an infected CD4 T cell over its lifespan.

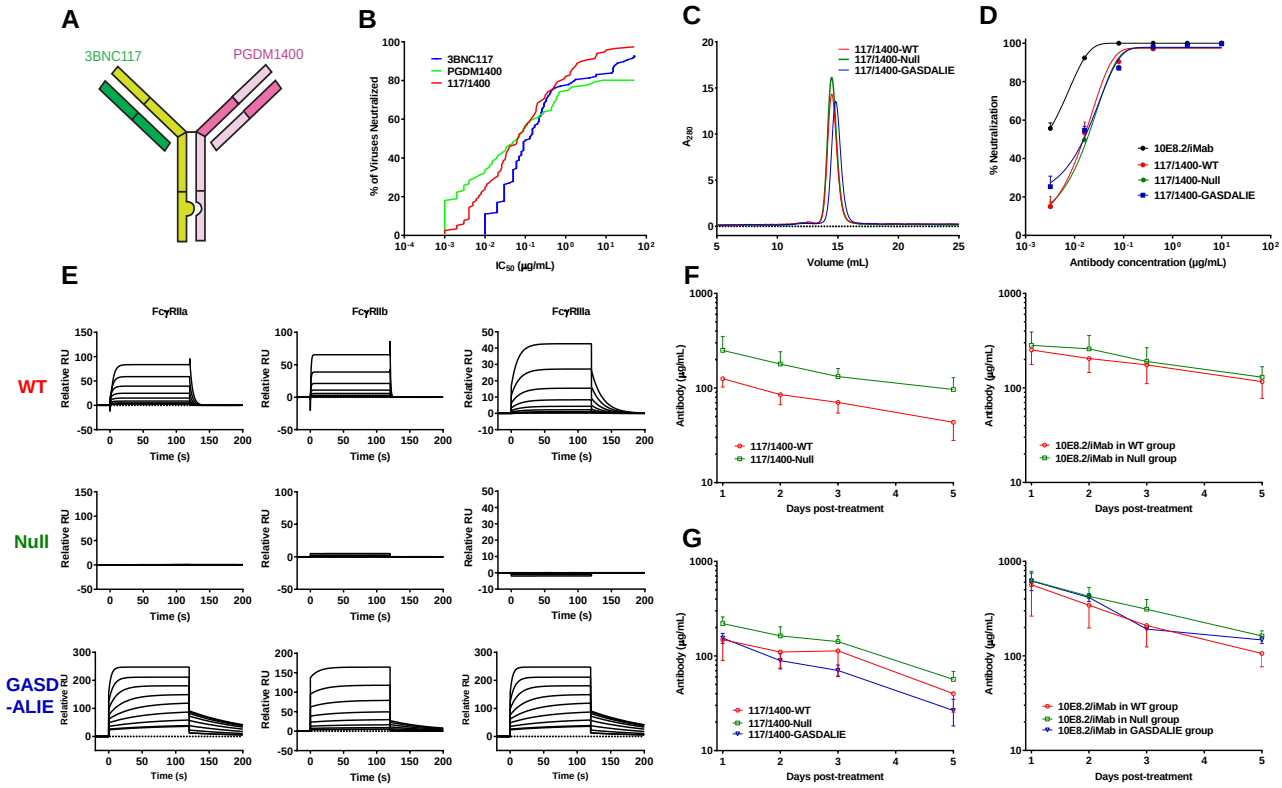

Fig. S2. *In vitro* characterization and *in vivo* PK profiles of 117/1400 variants and 10E8.2/iMab used for humanized mouse experiments. (A) A schematic depiction 117/1400. **(B)** Antiviral coverage of 117/1400 and its parental antibodies against a panel of 118 multi-clade HIV-1 strains. **(C)** Size exclusion chromatography (SEC) analysis of 117/1400 variants. **(D)** *In vitro* neutralization of HIV-1_{JR-CSF} by 117/1400 variants and 10E8.2/iMab. **(E)** Biacore sensograms of 117/1400 variants binding to human FcγRs. **(F** and **G)** PK profiles of 117/1400 variants and 10E8.2/iMab in the first **(F)** and second **(G)** experiment in HIV-1-infected humanized mice.

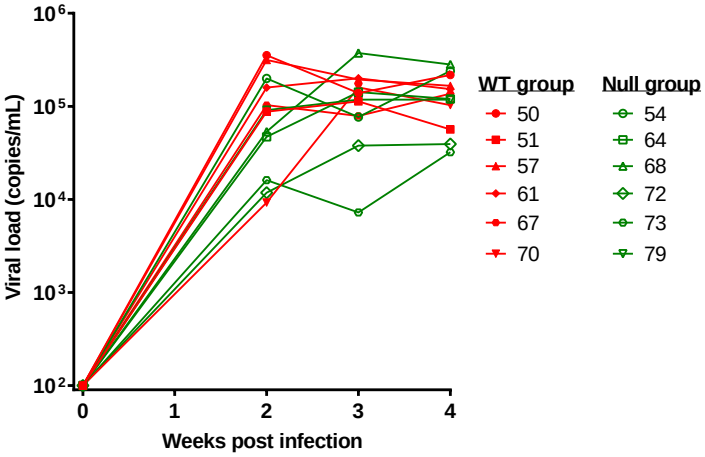

Fig. S3. Plasma viral load before antibody administration in the first humanized mouse experiment.

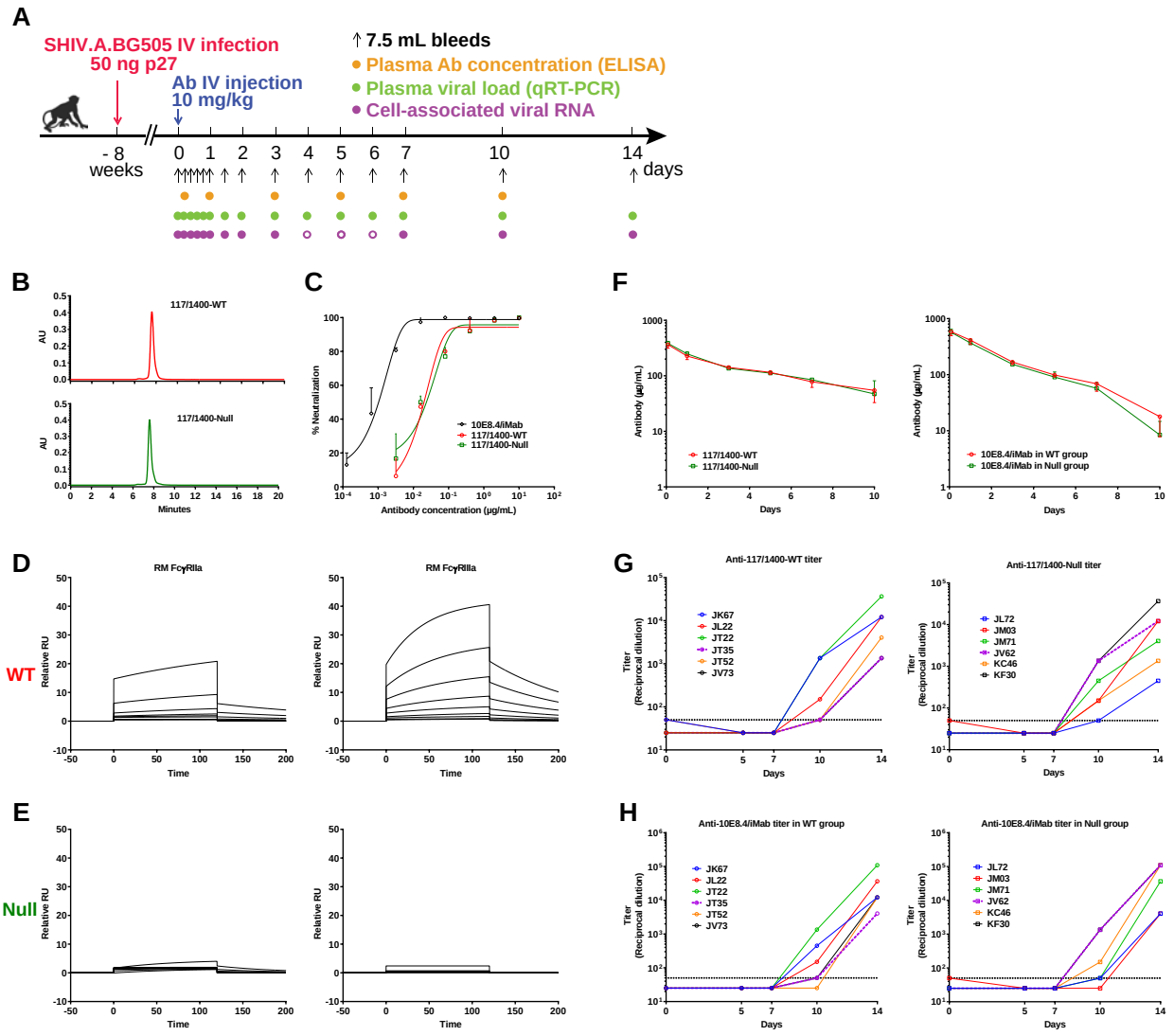

Fig. S4. *In vitro* characterization and *in vivo* PK profiles of 117/1400 variants and 10E8.4/iMab used for rhesus macaque experiments. (A) Experimental schema for the viral dynamics experiment performed in rhesus macaques. Open purple circles indicate time points when insufficient PBMCs were collected from some of the monkeys to measure cell-associated SHIV RNA. **(B)** SEC analysis of WT and Null variants of 117/1400 that were separately manufactured at Wuxi Biologics, Inc. **(C)** *In vitro* neutralization of SHIV.A.BG505 by 117/1400 variants, and by 10E8.4/iMab. **(D** and **E)**

Biacore sensograms of 117/1400 WT **(D)** and Null variants **(E)** binding to rhesus FcγRs. **(F)** PK profiles of 117/1400 variants and 10E8.4/iMab in the two groups of macaques. **(G** and **H)** Rhesus anti-human IgG response against 117/1400 **(G)** or 10E8.4/iMab **(H)** detected in serum by ELISA.

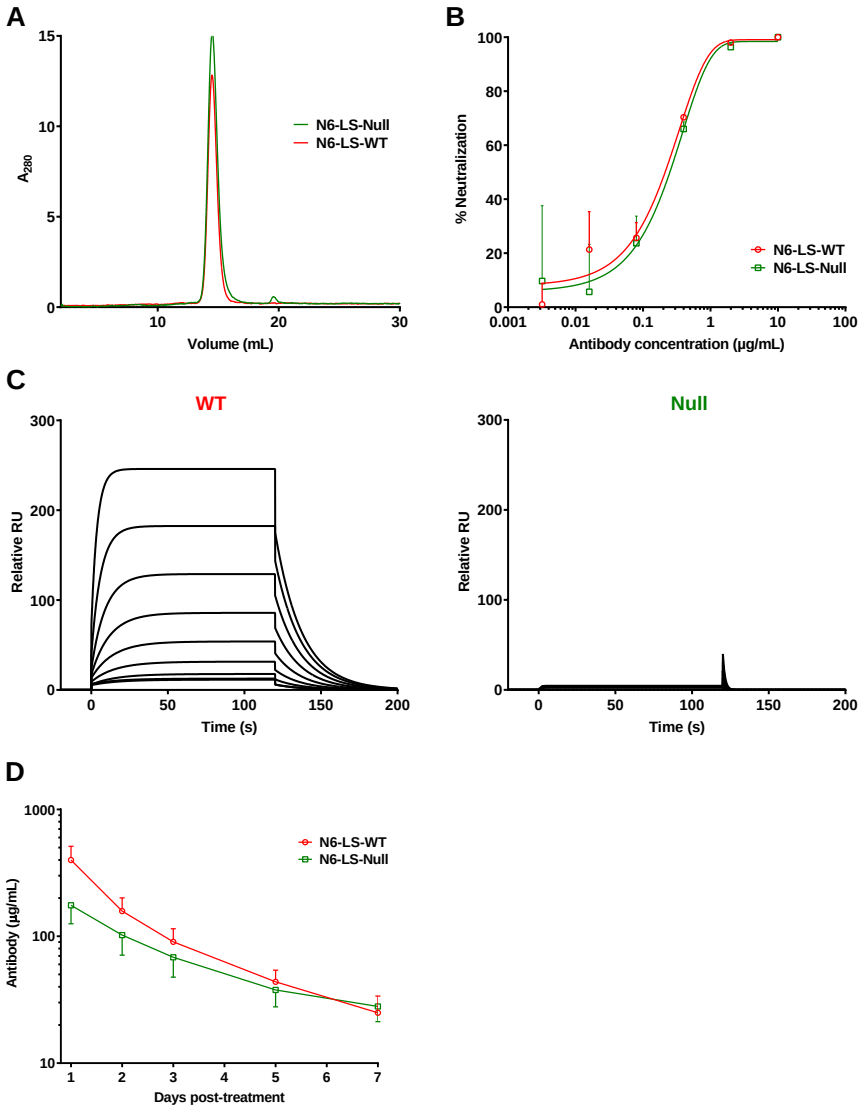

Fig. S5. *In vitro* characterization and *in vivo* PK profiles of N6-LS-WT and N6-LS-Null in the final humanized mouse experiment. (A) SEC analysis of N6-LS variants. **(B)** *In vitro* neutralization against HIV-$1_{pNL(AD8)}$ by N6-LS variants. **(C)** Biacore sensograms of N6-LS variants binding to human FcγRIIIa**. (D)** PK profiles of N6-LS-WT and N6-LS-Null in the final humanized mouse experiment.

Table S1: Baseline characteristics of HIV-1-infected humanized mice

1st Experiment

WT Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
50	Female	72.1	38.8	2.17×10^5
51	Female	81.6	65.7	5.65×10^4
57	Female	77.2	54.4	1.66×10^5
61	Male	54.8	63.5	1.53×10^5
67	Female	80.5	59.3	1.37×10^5
70	Male	62.0	68.8	1.03×10^5
Mean		**71.4**	**58.4**	**1.39×10^5**
Median				**1.45×10^5**

Null Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
54	Male	16.3	69.6	2.40×10^5
64	Female	77.9	49.9	1.20×10^5
68	Female	78.8	49.2	2.82×10^5
72	Female	71.2	74.4	3.94×10^4
73	Female	57.9	55.3	3.21×10^4
79	Female	80.7	60.5	1.18×10^5
Mean		**60.4**	**59.7**	**1.39×10^5**
Median				**1.19×10^5**

2nd Experiment

WT Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
3	Female	94.1	63.8	2.10×10^5
4	Female	89.8	44.0	6.24×10^4
32	Female	77.5	40.9	1.20×10^4
59	Male	50.1	55.5	7.32×10^5
82	Male	75.4	52.0	1.71×10^5
Mean		**77.4**	**51.2**	**2.38×10^5**
Median				**1.71×10^5**

Null Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
23	Female	75.9	61.6	1.37×10^5
60	Male	68.3	15.4	1.55×10^5
88	Female	80.6	50.6	2.97×10^5
89	Male	56.3	48.1	4.32×10^4
Mean		**70.3**	**43.9**	**1.58×10^5**
Median				**1.46×10^5**

GASDALIE Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
11	Male	73.8	57.0	9.14×10^4
14	Female	91.6	53.4	1.11×10^5
29	Female	28.8	78.5	1.36×10^6
91	Female	76.3	52.5	1.11×10^4
Mean		**67.6**	**60.4**	**3.94×10^5**
Median				**1.01×10^5**

3rd Experiment

WT Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
545	Male	61.4	49.9	5.99×10^6
556	Male	57.6	43.1	1.90×10^7
557	Male	61.1	43.6	1.76×10^6
559	Female	47.2	34.5	3.52×10^6
561	Female	70.0	41.8	3.94×10^6
562	Female	21.4	42.2	3.79×10^6
Mean		**53.1**	**42.5**	**6.34×10^6**
Median				**3.86×10^6**

Null Group				
Mouse #	Gender	% huCD45	% CD4	VL (copies /mL)
548	Female	70.8	54.1	4.26×10^6
549	Female	67.8	45.0	2.55×10^6
551	Female	59.9	47.2	4.04×10^6
554	Male	61.0	39.0	7.08×10^6
555	Male	46.6	43.7	1.38×10^7
558	Male	48.0	57.8	5.86×10^6
Mean		**59.0**	**47.8**	**6.36×10^6**
Median				**4.26×10^6**

Table S2: Baseline characteristics of SHIV-infected rhesus macaques

WT Group					
Animal #	Weight, Kg	Age	CD4 count (cells / µL)	VL (copies /mL)	TRIM5α allele
JK67	14.3	7.33	661	2.14×10^6	TFP/Q
JL22	15.0	7.32	534	3.35×10^4	TFP/TFP
JT22	14.2	7.09	810	1.25×10^4	TFP/Q
JT35	16.5	7.06	647	1.25×10^3	TFP/Q
JT52	16.0	7.07	786	1.45×10^4	TFP/Q
JV73	11.0	6.28	664	4.07×10^3	TFP/TFP
Mean	**14.5**	**7.03**	**684**	**3.68×10^5**	
Median				**1.35×10^4**	

Null Group					
Animal #	Weight, Kg	Age	CD4 count (cells / µL)	VL (copies /mL)	TRIM5α allele
JL72	15.5	7.30	462	3.66×10^3	TFP/Q
JM03	14.0	7.29	1042	9.90×10^2	TFP/Q
JM71	11.7	7.28	586	3.11×10^4	TFP/Q
JV62	16.0	6.42	1193	7.04×10^5	TFP/Q
KC46	12.1	6.28	646	2.13×10^4	TFP/TFP
KF30	14.1	6.24	560	6.45×10^3	TFP/Q
Mean	**13.9**	**6.80**	**748**	**1.28×10^5**	
Median				**1.39×10^4**	