

Supplemental Material for

## **Polyreactivity and Autoreactivity among HIV-1 Antibodies**

Mengfei Liu<sup>a\*</sup>, Guang Yang<sup>b</sup>, Kevin Wiehe<sup>c</sup>, Nathan I. Nicely<sup>c</sup>, Nathan A. Vandergrift<sup>c</sup>, Wes Rountree<sup>c</sup>, Mattia Bonsignori<sup>c,d</sup>, S. Munir Alam<sup>c</sup>, Jingyun Gao<sup>a†</sup>, Barton F. Haynes<sup>b,c,d</sup>, and Garnett Kelsoe<sup>b,c#</sup>

School of Medicine<sup>a</sup>; Department of Immunology<sup>b</sup>; Human Vaccine Institute<sup>c</sup>, and Department of Medicine<sup>d</sup>, Duke University, Durham, North Carolina, USA

Running Head: Poly- and Autoreactivity of HIV-1 Antibodies

#Address correspondence to Garnett Kelsoe, ghkelsoe@duke.edu.

\*Present address: Mengfei Liu, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

†Present address: Jingyun Gao, University of Chicago Medical Center, Chicago, Illinois

M.L. and G.Y. contributed equally to this work.

Table 1: bNAbs\*

Viral Epitope	Clonal Family		bNAb or nNAb	V <sub>H</sub>	HCDR3 Length	V <sub>H</sub> Mut (%nt)	Isotype	V <sub>L</sub>	LCDR3 Length	V <sub>L</sub> Mut (%nt)	Source	Derived	Neutralization Breadth <sup>†</sup>	Neutralization Potency <sup>‡</sup>	Auto- or polyreactivity <sup>**</sup>	References
CD4bs	VRC01-03	VRC01	bNAb	1-2	14	32	IgG1	K3-20	5	17	chronic infection 45	rAb	++++	+++	Autoreactive (UBE3A)	(1)
		VRC02	bNAb	1-2	14	32	IgG1	K3-20	5	19			++++	+++	-	(1)
		VRC03	bNAb	1-2	16	30	IgG1	K3-20	5	20			++++	+++	-	(1)
		VRC07	bNAb	1-2	16	35.7	IgG1	K3-20	5	17			++++	+++	Polyreactive	(2, 3)
		NIH45-46	bNAb	1-2	16	30	IgG1	K3-20	5	--			++++	+++	Polyreactive	(4)
	CH98	CH98	bNAb	3-30	21	25.3	IgG1	L2-23	5	16	chronic infection w SLE CH5329	rAb	++	NR	Polyreactive	(5)
	VRC-CH30-34	CH31	bNAb	1-2	13	24	IgG1	K1-33	5	15	chronic infection 0219	rAb	+++	+++	Polyreactive	(6, 7)
	CH103-106	CH103	bNAb	4-59	15	15.1	IgG1	L3-1	10	12	Infected CH505	rAb	++	++	Polyreactive	(8)
CH106		bNAb	4-59	15	16	IgG1	L3-1	10	11.2	++			++	Polyreactive	(8)	
MPER	2F5	2F5	bNAb	2-5	22	14	IgG3	K1-13	9	11.8	Infected	hybridoma/rAb	++	++	Autoreactive (KYNU, CMTM3)	(9, 10)
	4E10	4E10	bNAb	1-69	18	14	IgG3	K3-20	9	10.5	Infected	hybridoma/rAb	++++	++	Polyreactive	(10-12)
	10E8	10E8	bNAb	3-15	20	21	IgG3	L3-19	12	14	Infected N152	rAb	++++	+++	Autoreactive (FAM84A)	(13)
	CAP206-CH12	CH12	bNAb	1-69	15	12	IgG1	K3-20	11	5	Chronic infection CAP206	rAb	+	++	-	(12)
V1V2-glycan	PG9, PG16	PG9	bNAb	3-33	28	14.9	IgG1	L2-14	11	10.1	Chronic infection	rAb	+++	+++	Polyreactive	(14-16)
		PG16	bNAb	3-33	28	14.5	IgG1	L2-14	11	12.5			+++	+++	-	(14-16)
	CH01-04	CH01	bNAb	3-20	24	13.3	IgG1	K3-20	9	10	Chronic infection CH0219	rAb	+	++	-	(17)
		CH03	bNAb	3-20	24	12	IgG1	K3-20	9	10.6			+	++	-	(17)
	PGT141-145	PGT145	bNAb	1-8	31	18	NR	K2-28	9	16	chronic infection 84	rAb	+++	+++	-	(18)
V3-glycan	2G12	2G12	bNAb	3-21	14	21	IgG1	K1-5	9	18.4	Infected	hybridoma/rAb	+	++	-	(9, 19, 20)
	PGT121-123	PGT121	bNAb	4-59	24	17	NR	L3-21	12	18	chronic infection 17	rAb	++	++++	-	(18)
	PGT125-131	PGT125	bNAb	4-39	19	20	NR	L2-8	10	15	chronic infection 36	rAb	++	++++	Polyreactive	(18)
		PGT128	bNAb	4-39	19	19	NR	L2-8	10	14			++	++++	Polyreactive	(18)

Table 2: nNAb\*s

Viral Epitope	Clonal Family		bNAb or nNAb	V <sub>H</sub>	HCDR3 Length	V <sub>H</sub> Mut (%nt)	Isotype	V <sub>L</sub>	LCDR3 Length	V <sub>L</sub> Mut (%nt)	Source	Derived	Neutralization Breadth <sup>†</sup>	Neutralization Potency <sup>‡</sup>	Auto- or polyreactivity <sup>**</sup>	References
<b>V2 linear</b>	<b>CH58</b>	<b>CH58</b>	nNAb	5-51	19	1.8	IgG1	6-57	9	1.8	RV144 vaccinee 347759	rAb	-	-	-	(21)
<b>V2 linear</b>	<b>CH59</b>	<b>CH59</b>	nNAb	3-9	13	2.8	IgG1	3-10	11	0.9		rAb	-	-	-	(21)
<b>V2</b>	<b>HG107</b>	<b>HG107</b>	nNAb	3-9	14	2.3	IgG1	3-10	10	0.9	RV144 vaccinee 200134	rAb	-	-	-	(21)
<b>V2</b>	<b>HG131</b>	<b>HG131</b>	nNAb	3-30	13	5.2%	IgG1	L3-25	10	2.9%	RV144 vaccinee 302689	rAb	-	-	Polyreactive	Bonsignori <i>et al</i> unpublished
<b>V3 loop</b>	<b>F39F</b>	<b>F39F</b>	nNAb								Infected		-	-	Autoreactive (PACRG1)	(22)
<b>V3 loop</b>	<b>19b</b>	<b>19b</b>	nNAb				IgG1				Infected N70	EBV	-	-	-	(23, 24)
<b>C1</b>	<b>A32</b>	<b>A32</b>	nNAb	4-30	15	10.3%	IgG1	L2-8	10	5.1%	Infected			-	-	(25)
<b>CD4i</b>	<b>17b</b>	<b>17b</b>	nNAb	1-69	19	27 (V <sub>JH</sub> and V <sub>JL</sub> )	IgG1	K2	12	27 (V <sub>JH</sub> and V <sub>JL</sub> )	Infected			-	-	(22)
<b>CD4i</b>	<b>48d</b>	<b>48d</b>	nNAb	1-24	10	23 (V <sub>JH</sub> and V <sub>JL</sub> )	IgG1	K19	8	23 (V <sub>JH</sub> and V <sub>JL</sub> )	Infected			-	-	(22)

\*Adapted from (26).

<sup>†</sup> Adapted from (26). Breadth indicated for Abs tested on large panels of >100 tier 2 Env pseudoviruses. Values indicate percentage of viruses that were neutralized at an IC<sub>50</sub> < 50 µg/ml: +++++ ≥90%; +++ = 75-90%; ++ = 50-74%; + ≤50%; - indicates no neutralization of diverse tier 2 viruses.

<sup>‡</sup> Adapted from (26). Potency indicated by mean IC<sub>50</sub> (µg/ml) of neutralized viruses: +++++, <0.05; +++ = 0.05-0.49; ++ = 0.5-4.9; + = 5.0-50.

\*\*Polyreactivity and Autoreactivity determined using protein microarray (Figs. 5, 6). Polyreactive Abs bind all array proteins on average >2-fold more avidly than control 151K (PI > 0.21); autoreactive Abs are not polyreactive (PI ≤ 0.21), but bind specific array proteins ≥500-fold stronger than 151K.

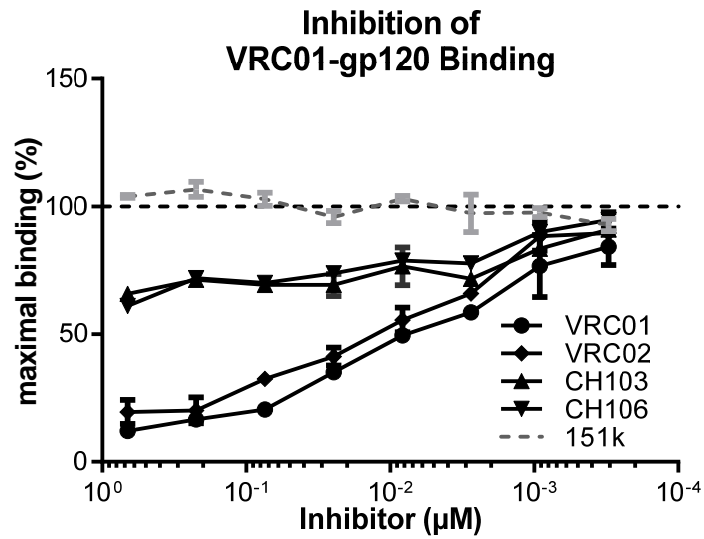


Fig. S1. Inhibition of VRC01 binding to gp120 by VRC01, VRC02, CH106, CH103, and 151K assessed in ELISA as described in Materials and methods. The y-axis indicates OD percentage of maximal binding, which is determined as the mean reading without inhibitors (dashed line). X-axis depicts molar concentration of inhibitor bNAbs. Error bars indicate standard deviation.

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