

Fig S1. Levels of anti-VRC01 antibodies Mean \pm SEM of the endpoint titers of anti-VRC01 antibodies in the VRC01-alone and VRC01- $\alpha_4\beta_7$ group are shown at baseline and for the first 8 weeks past-infusion.





Fig S2. No difference in peak plasma viral load among the treatment groups. Highest level of SIV RNA copies in plasma reached within the first 5 weeks of infection in each animal is shown.



Fig S3. No difference in vaginal tissue viral load among the treatment groups. Copies of SIV DNA (A) and RNA (B) from vaginal biopsies at the indicated times after infection were quantified by gag-qPCR (normalized on albumin content) and by RT-qPCR (normalized on RNA content) respectively. The dotted line indicates the lower limit of detection (LLOD) of the assay.



Fig S4. SIV DNA loads in different tissues at necropsy. Viral DNA loads in each tissue were measured by SIV gag qPCR and normalized on albumin copies. The dotted line indicates the lower limit of detection (LLOD) of the assay.





Fig S5 Rh- $\alpha_4\beta_7$ -VRC01-treated macaques have higher levels of circulating CCR6+ CD4+ T cells in the chronic phase. Around week 20 p.i. blood T cells were phenotyped by flow cytometry. The frequency of the subset that significantly differed among the treatment group is shown. The results of the Dunn's multiple comparisons post-hoc test (after the Kruskal-Wallis test controlled for multiple comparisons) and the Mann-Whitney test to compare the treatment groups between each other are shown (*p*-value of * α <0.05, was considered significant).

Fig S6 Blood T cell responses the against consensus Β envelope peptide pool. PBMCs isolated around 18 weeks post infection were stimulated with pooled 15-mer peptides with an 11aa overlap from the consensus B envelope protein for 5hrs. The frequency of cells secreting the indicated cytokines are shown for the CD4⁺ and CD8⁺ T cell subsets after subtraction of the baseline values (in absence of peptides). The results of the Dunn's multiple comparisons post-hoc test (after the Kruskal-Wallis test controlled for multiple comparisons) and the Mann-Whitney test to compare the treatment groups between each other are shown (p-value of * α<0.05. ** α<0.01 and *** α<0.001 were considered significant).



Majority	QEVVLENVTENFN	IMWKNNMVEQMHEDI	ISLWDQ	SLKPCVKLTPLCVT		XXNXTNXXXXSSX	EXMXXGELI	KNCSFNI
	90	100	110	120	130	140	150	160
Consensus B env protein.pro SHIV_AD8 ENV.pro	QEVVLENVTENFN	MWKNNMVEQMHEDI	ISLWDQ 	SLKPCVŔLTPLCVT	I NCT DI	LMNATNTTNSSSG AG.V.IN.S	EKMEKGELI . E R	KNCSFNI 160
Majority	TTSI RDKVXXXYA	LFYXLDVVPI DNDN	TSXYRL	I SCNTSXI TQACPK	VSFEPI	I PI HYCXPAGFAI		NGTGPCX
	170	180	190	200	210	220	230	240
Consensus B env protein.pro SHIV_AD8 ENV.pro	TTSI RDKVQKEYA	LFYKLDVVPI DNDN	TE SYRL	I SCNTSVI TQACPK	VSFEPI	I PI HYCAPAGFAI	LKCNDKKFI	NGTGPCT 240

Fig S7. Alignment of the V1-V2 region of the consensus B and SHIV_{AD8-EO} **envelope sequences.** Peptides of 20aa (overlapping 14aa) spanning the region shown in yellow were synthetized and used to probe T cell and antibody responses.





Fig S8. Peptide scan. Serum from 4 animals from each treatment group was analyzed by peptide scan against consensus B envelope peptides. 7 SHIV-AD8-specific peptides replaced the corresponding peptides in the V1-V2 loop region.

PBMC acute	Color	Clone	Manufacturer
CD3	V450	SP34-2	BD Biosciences
CD4	BUV395	L200	BD Biosciences
CD95	PercP-Fluor710	DX2	eBioscience
CCR6	PE-Dazzle 594	G034E3	BioLegend
NKG2A	PE	REA110	Miltenyi
alpha4	AF700	7.2R	Novus Biologicals
CXCR3	AF488	G025H7	BioLegend
IL-17A	PE-Cy7	Ebio64DEC17	eBioscience
P27	AF647H	2F12	NIAIDS
CCR7	BV605	G043H7	BioLegend
IFNg	APC-efluor780	4S.B3	eBioscience

RECTAL acute	Color	Clone	Manufacturer
CD3	V450	SP34-2	BD Biosciences
CD4	BUV395	L200	BD Biosciences
NKp44	PercP-Cy5.5	P44	BioLegend
CCR6	PE-Dazzle 594	G034E3	BioLegend
alpha4	PE	7.2R	Novus Biologicals
CXCR3	AF488	G025H7	BioLegend
IL-17A	PE-Cy7	Ebio64DEC17	eBioscience
NKG2A	APC	REA110	Miltenyi
CD20	AF700	2H7	BD Biosciences
lgA	In house APC-Cy7	10F12	NHPR center

PBMC stimulation	Color	Clone	Manufacturer
CD3	V450	SP34-2	BD Biosciences
CD8	PE-CF594	RPA-T8	BD Biosciences
CD4	BUV395	L200	BD Biosciences
NKG2A	PE Vio 770	REA110	Miltenyi
IL-17A	APC-eFluor 780	eBio64DEC17	eBioscience
IFN-gamma	AF700	B27	BD Biosciences
IL-2	Brilliant Violet 605	MQ1-17H12	BioLegend
IL-21	APC	3A3-N2	BioLegend
IL-22	PerCP-eFluor 710	IL22JOP	eBioscience
TNF alpha	FITC	MAb11	BioLegend

Tissue stimulation	Color	Clone	Manufacturer
CD3	V450	SP34-2	BD Biosciences
CD8	PE-CF594	RPA-T8	BD Biosciences
CD4	BUV395	L200	BD Biosciences
NKp44(CD336)	PerCP-Cy5.5	P44-8	BioLegend
CCR6 (DcR2)	PE-Cy7	G034E3	BioLegend
TNF alpha	FITC	MAb11	BioLegend
IL-17A	APC-eFluor 780	eBio64DEC17	eBioscience
IFN-gamma	Alexa Fluor 700	B27	BD Biosciences
IL-2	BV 605	MQ1-17H12	BioLegend
IL-21	PE	3A3-N2	BioLegend
p27	APC	2F12	

PBMC (chronic) Color Clone Manufacturer **BD** Biosciences CD3 Alexa Fluor 700 SP34-2 CD4 BUV395 L200 **BD** Biosciences CXCR5 FITC 710D82.1 NHP CXCR3 PerCP-Cy5.5 G025H7 **BD** Biosciences CD95 V450 DX2 **BD** Biosciences CD127 PE-Cy7 eBioRDR5 eBioscience CD25 APC-eFluor 780 BC96 BioLegend CCR6 PE-Dazzle 594 G034E3 BioLegend CD103 ΡE B-Ly7 eBioscience CD69 Brilliant Violet 605 FN50 **BD** Biosciences P27 APC 2F12 NIAIDS

LN (chronic)	Color/Format	Clone	
CD3	Alexa Fluor 700	SP34-2	BD Biosciences
CD4	BUV395	L200	BD Biosciences
CXCR5	FITC	710D82.1	NHPR program
CXCR3	PerCP-Cy5.5	G025H7	BD Biosciences
CD95	V450	DX2	BD Biosciences
CD127	PE-Cy7	eBioRDR5	eBioscience
CD25	APC-eFluor 780	BC96	BioLegend
CCR6	PE-Dazzle 594	G034E3	BioLegend
PD-1	PE	EH12.2H7	BioLegend
CD69	Brilliant Violet 605	FN50	BD Biosciences
P27	APC	2F12	NIAIDS

Fig S9. Panels used for flow cytometry analysis of cell subset and T cell responses. Acute analysis were done with samples collected at week 3 or 4 postinfection, while chornic samples were collected from week 18 to 22 postinfection.