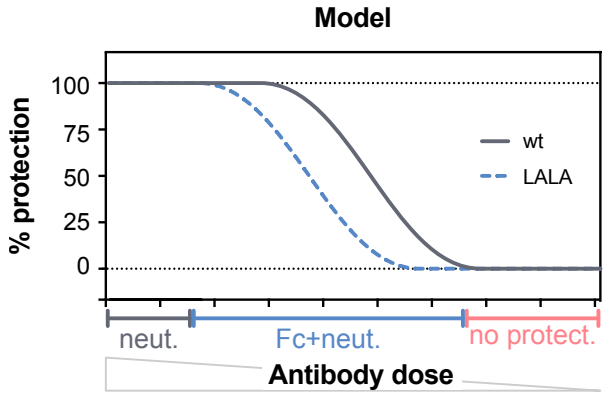

Fig. S1. Hypothesis for possible effector function augmentation in relation to antibody concentration.

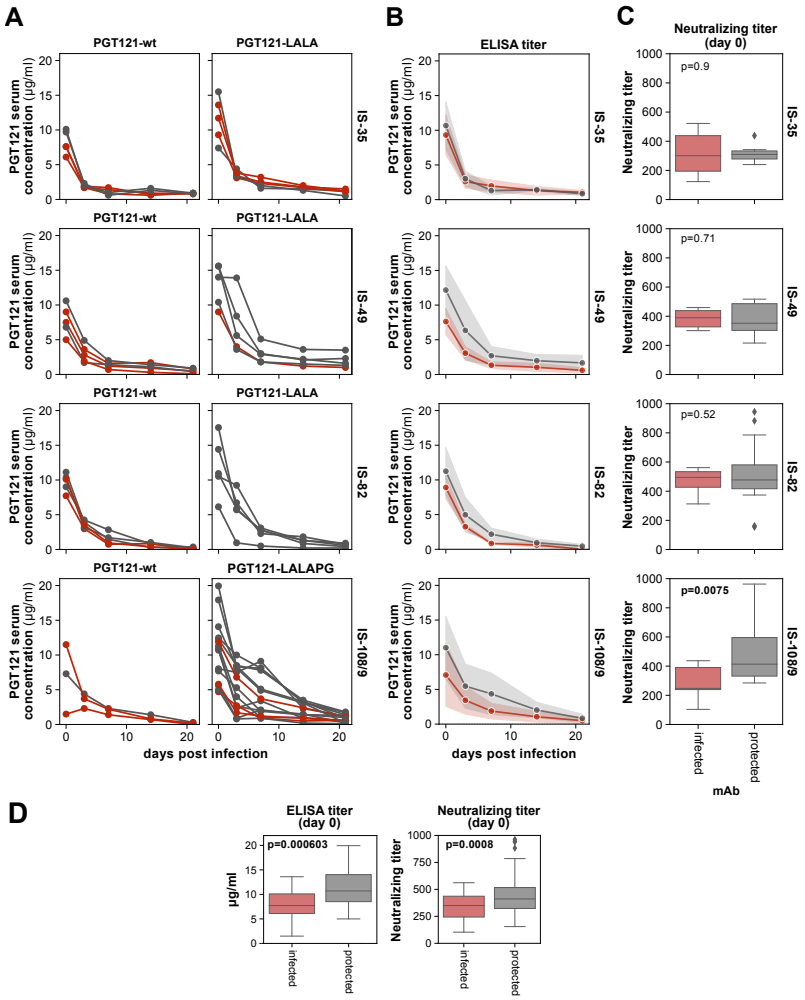

Fig. S2. PGT121 serum antibody titers. (A) Individual macaque PGT121 serum concentrations were measured over time. HIV-specific IgG was detected by ELISA and EC_{50} values were determined using non-linear regression and translated into concentrations using wild type (wt) PGT121 standards. Protected animals are indicated in gray, infected animals that were viremic at any point are indicated in red. **(B)** Serum concentrations were compared between wild-type and Fc-crippled variants displayed in (A) binned by the outcome of the challenge, and plotted as mean values over time with the corresponding standard deviation indicated as a semi-transparent band. **(C)** $SHIV_{SF162P3}$ pseudovirus serum neutralizing titers on the day of infection were evaluated and binned by outcome. Data were plotted as median (line) interquartile (box) and 1.5x interquartile range (whiskers). Outliers are indicated as diamonds and indicated p values were determined by Welch two sample t-tests. **(D)** Day 0 ELISA and neutralizing antibody titers were plotted by outcome. Data from B and C were binned according to outcome and plotted as above. Indicated p values were determined by Welch two sample t-tests.

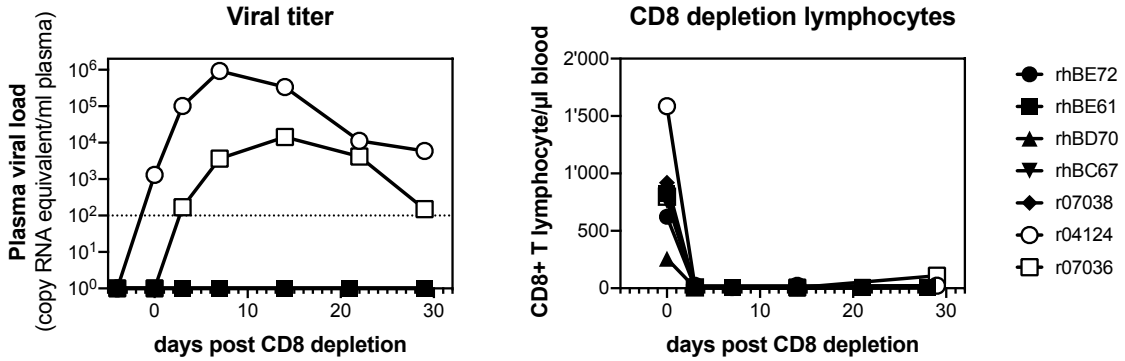

Fig. S3. CD8 depletion to probe presence of virus in antibody-treated macaques. Blood viremia (left panel) was quantified following depletion of $CD8^+$ T cells. Animals had previously received wild-type or LALA PGT121 and either remained uninfected (bold face symbols) or became infected and spontaneously controlled viremia. 482 days post infection, $CD8^+$ T cells were depleted by a single injection of 50 mg/kg of mAb cM-T807 on day 0. Successful depletion of $CD8^+$ cells was confirmed 3 days post treatment by flow cytometry (right panel).

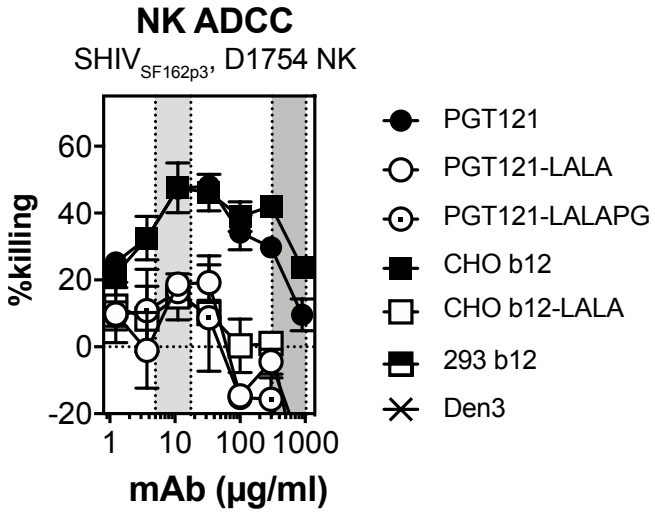

Fig. S4. Additional in vitro ADCC assay. Human NK cell ADCC (donor D1754) was measured in vitro with Ab concentrations up to those measured in passive immunization experiments. Light and dark gray areas indicate the serum concentration range present on day 0 in PGT121 and b12 protection experiments, respectively.

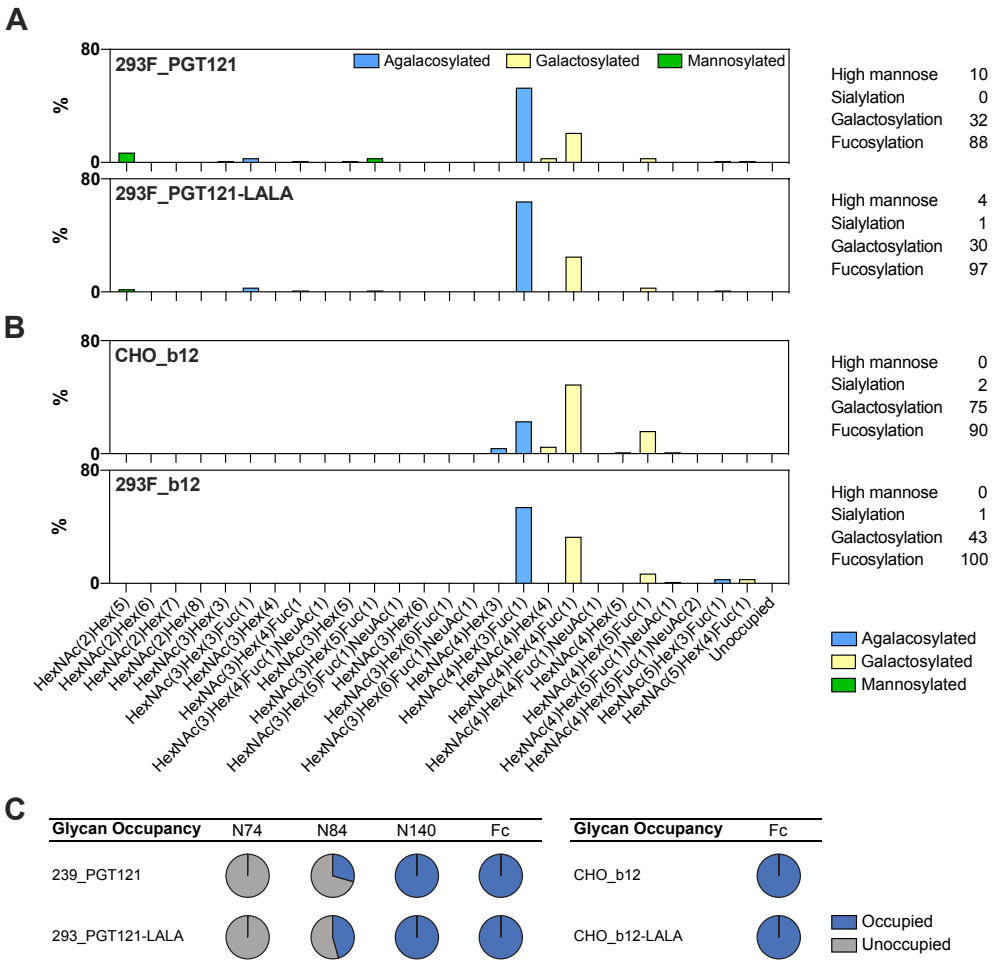

Fig. S5. Glycoanalyses of CHO-produced b12 and 293F cell-produced PGT121 variants. Antibody glycosylation and occupancy was determined using liquid chromatography-mass spectrometry (LC-MS). The PGT121 heavy chain contains 4 glycosylation sites, three sites in the Fab region (N74, N84 and N140) and one in the Fc, while b12 contains just the Fc site. **(A)** Relative quantification of glycosylation present on the Fc glycan of PGT121 produced in HEK293F, and impact of LALA mutation. The different glycan compositions detected across all antibodies are shown on the x-axis. Hex refers to a hexose monosaccharide and HexNAc refers to a hexosamine monosaccharide. LALA mutations had only a small impact upon Fc glycosylation. **(B)** Relative quantification of glycosylation present on the Fc glycan of b12 produced in CHO and HEK 293F cells. CHO-expressed b12 displayed a glycosylation pattern that differed from that observed on PGT121. **(C)** Occupancy of glycosylation sites. The relative chromatographic areas were compared for a single peptide sequence with different post translational modifications to determine the proportion of N-linked glycan sites occupied and those lacking a glycan. Unoccupied peptides could not be detected for N140 and for the conserved Fc glycan site. No unoccupied peptides were detected for b12 expressed in CHO cells with or without LALA mutations.

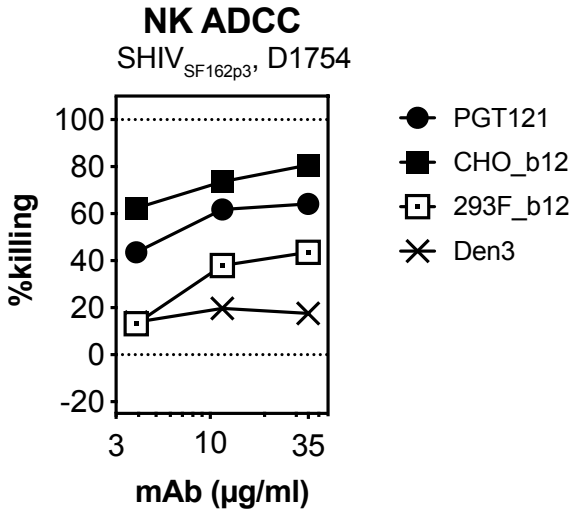

Fig. S6. Effect of producer cell line on ADCC activity. Human NK ADCC activity (donor D1754) against $SHIV_{SF162p3}$ infected target cells was measured using mAbs produced in the indicated cell lines.

Table S1. Assessment of T cell priming in protected animals. Using frozen peripheral blood mononuclear cells and the assays indicated, the presence of T cells specific for the indicated epitopes was assessed by tetramer and intracellular cytokine staining (ICS). For tetramer stains, the percentages of live $CD3^+$ $CD8^+$ $tetramer^+$ lymphocytes are indicated while for ICS frequencies were calculated as responding $CD4^+$ or $CD8^+$ T-cells (i.e. $CD14^-$ $CD16^-$ $CD20^-$ $CD3^+$ lymphocytes of either subset producing any combination of IFN-γ, TNF-α, or CD107a together with CD69). Infected animals are indicated with an asterisk.

Mamu-A*02 tetramer

ID	treatment	dpi	**Gag GY9** (71-79)	**Vif WY8** (97-104)	**Nef YY9** (159-167)	**Env RY9 (296-304)**	**Env RY8 (788-795)**
rhBD70	PGT121-LALA	d219	0.003	0.005	0.000		
rhBD98*	DEN3	d219	**0.410**	**1.300**	0.008		
rhBE31*	PGT121-LALA	d219	**0.620**	**0.054**	**0.034**		
rhBB23*	DEN3	d219	0.075	0.000	0.002		
r08026	PGT121-LALA	d-1		0.012	0.000	0.008	0.048
r08026*	PGT121-LALA	d177		0.009	0.000	0.012	0.047
r08047	SIV-infected			**0.706**	**0.039**	**2.680**	**0.075**
rh2580	pre-infection	d-1	0.200	0.007	0.000	**0.015**	
rh2580	PGT121-LALA	d177	0.097	0.002	0.000	0.008	
r08047*	SIV infected		**0.294**	**0.706**	**0.039**	**2.680**	

Mamu-B*17 tetramer

ID	treatment	dpi	**Nef IW9** (165-173)	**Nef MW9** (195-203)	**Vif HW8** (66-73)
r03055*	PGT121	177	**0.180**	**0.005**	**0.007**
r09033*	PGT121	177	**0.830**	0.000	**0.015**
r04124*	PGT121	219	**1.400**	0.000	**0.190**
rhBB23*	DEN3	219	**0.700**	**0.002**	**0.011**
rhBD70	PGT121-LALA	219	0.003	**0.003**	0.003

Mamu-B*17 tetramer

ID	treatment	dpi	**Nef IW9** (165-173)	**Nef MW9** (195-203)	**Vif HW8** (66-73)
r08026	PGT121-LALA	-1	0.000	0.000	0.000
r08026*	PGT121-LALA	177	0.000	**0.003**	0.000
r08047	SIV-infected		0.000	**0.803**	**0.024**

Mamu-B*08 tetramer

ID	treatment	dpi	**Vif RL8** (173-181)	**Nef RL9a** (8-16)	**Vif RL9** (123-131)	**Nef RL10** (137-146)	**Rev KL9** (12-20)	**Rev RL8** (44-51)
r07036*	PGT121	219	**0.390**	0.003	**0.840**	**1.100**	0.003	0.015

Intracellular IFN-gamma and TNF-alpha

ID	treatment	dpi	no stimulus	**PMA/Ionomycin**	**Gag** (1-263)	**Vif** (whole ORF)	**Nef** (whole ORF)
r08026*, CD8+	PGT121-LALA	177	0.000	9.430	0.000	0.004	0.005
r08026*, CD4+	PGT121-LALA		0.000	5.130	0.002	0.000	0.000
r97104, CD8+	PGT121-LALA	177	0.000	12.1	0.02	0.01	0.005
r97104, CD4+	PGT121-LALA		0.000	5.88	0.000	0.001	0.002
rh2580, CD8+	PGT121	177	0.000	17.500	0.003	0.000	0.003
rh2580, CD4+	PGT121		0.000	9.330	0.004	0.002	0.005
rh2581, CD8+	PGT121	177	0.009	7.960	0.000	0.000	0.005
rh2581, CD4+	PGT121		0.000	8.690	0.000	0.000	0.004