Supplementary Data:

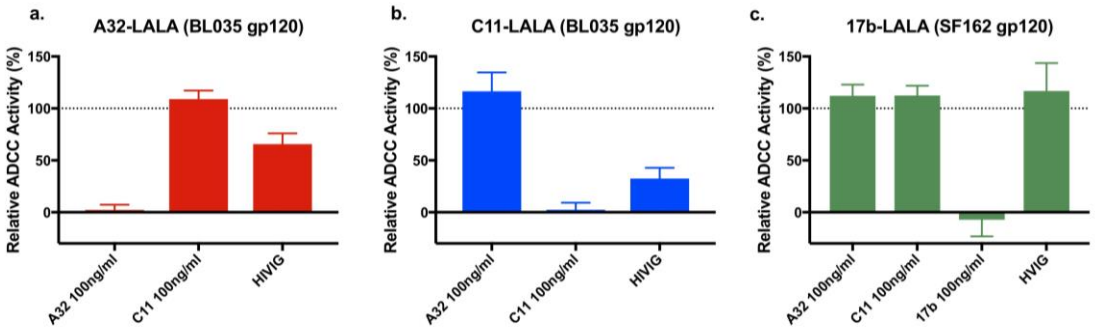

Fig. S1. Validation of LALA antibodies in the competition RFADCC assay
25µg/ml A32-LALA (a), 25µg/ml C11-LALA (b), or 5µg/ml 17b-LALA (c) was pre-incubated with target cells in the competition RFADCC assay. Target cells in the A32-LALA and C11-LALA competition ADCC assays were coated with clade A/D BL035 gp120. Target cells in the 17b-LALA competitive ADCC assay were coated with clade B SF162 gp120. Relative ADCC mediated by fully functional A32, C11, and 17b antibodies (100ng/ml) or the positive control HIVIG (1:5000 dilution) in the presence of each LALA antibody is shown. Relative ADCC is defined as ADCC in the presence of the LALA variant normalized to ADCC in an equivalent volume of media (represented by the dashed line at 100%). Error bars represent mean+SD. Results are averaged from six replicates (a and b) or eight replicates (c).

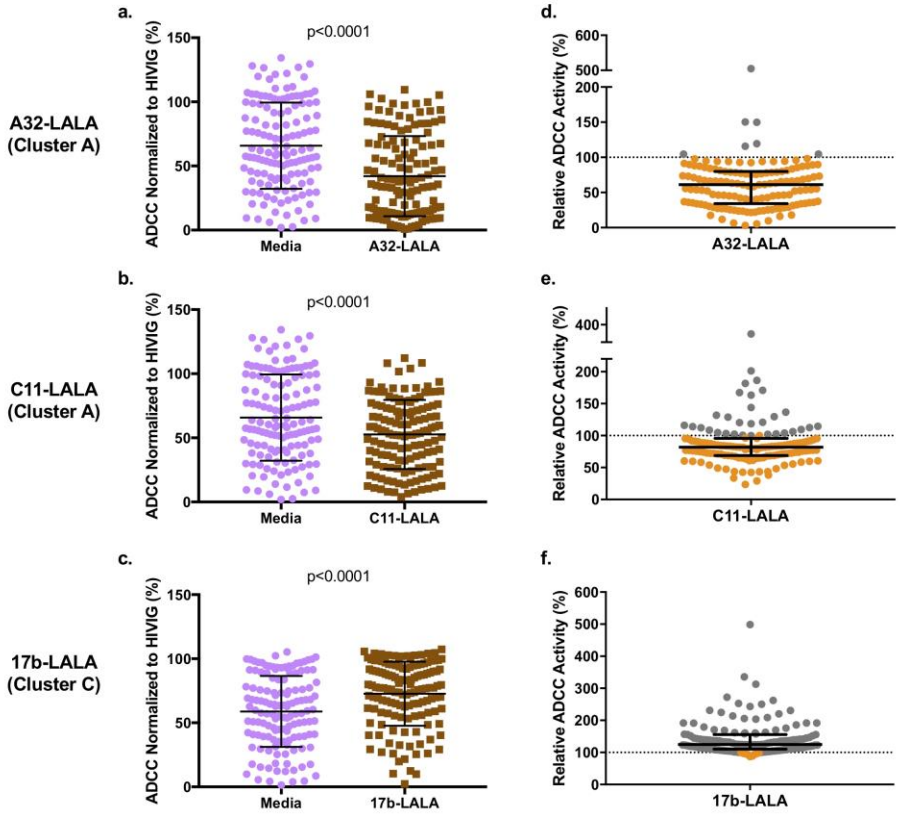

Fig. S2. Incubation of samples with LALA antibody variants affects plasma RFADCC activity
Results of the competition RFADCC assay performed on 142 plasma samples from breastfeeding Kenyan mother-infant pairs. a-c: RFADCC activity (normalized to the positive control HIVIG) of plasma samples in the presence of media only (purple) or in the presence of a LALA variant (brown). RFADCC activity in the presence of media or the LALA variant were compared by a paired t test. P-values are shown. Statistical significance was defined as $p<0.05$. Error bars represent mean+SD. d-f: Relative ADCC of each plasma sample in the presence of A32-LALA (d), C11-LALA (e), or 17b-LALA (f) normalized to ADCC in the presence of media alone (dotted line at 100%) is shown. Orange dots show samples that had RFADCC activity inhibited by the LALA variant. Gray dots show samples that had RFADCC activity enhanced by the LALA variant. Results are averaged from two biological replicates. Error bars represent median+IQR. Data from individual biological replicates from seven maternal samples and six infant samples that were below the limit of detection were excluded from the analysis as described in the Materials and Methods.

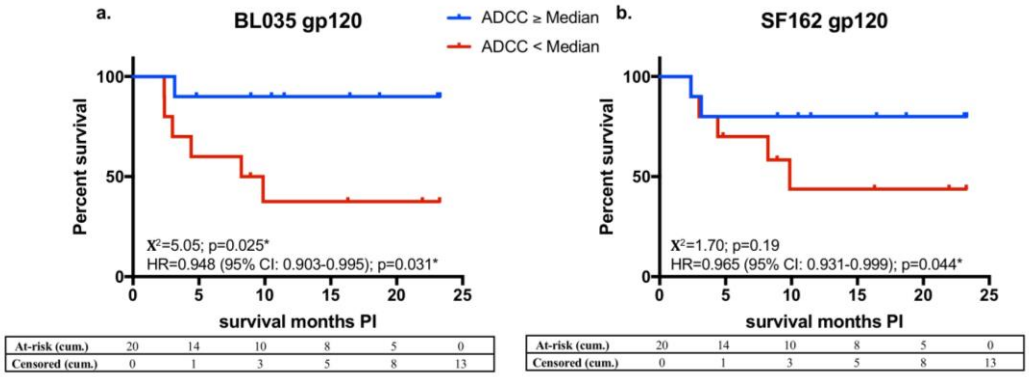

Fig. S3. Association of passively-acquired ADCC with HIV+ infant survival using two different gp120 antigens.

Passively acquired ADCC in HIV+ infant plasma (N=20) was measured in the control (no LALA competitor) condition of the competition RFADCC assay (1:5000 dilution of plasma added to target cells pre-incubated with media only). Target cells were coated with clade A/D BL035 gp120 (a) or clade B SF162 gp120 (b). Kaplan-Meier survival curves between infants that had passively-acquired ADCC at/above the HIV-infected infant cohort median (blue lines) or below the HIV-infected infant cohort median (red lines) were compared by a log-rank test (X^2 values and p-values are shown). The x-axis shows months survival post infection (PI). The association of passively-acquired ADCC with risk of HIV+ infant mortality was measured by a Cox-proportional hazards model. Hazard ratios (HR), 95% confidence intervals (CI), and p-values are shown on the graphs. Statistical significance was defined as $p<0{\cdot}05$ (*). Cumulative (cum.) number of infants at-risk or censored by the end of each month on the x-axis are shown in the tables. Data from an individual biological replicate from one infant sample that was below the limit of detection was excluded from the analysis as described in the Materials and Methods.

	Passively-Acquired ADCC			Maternal ADCC		
	Adjusted HR	**95% CI**	**p-value**	**Adjusted HR**	**95% CI**	**p-value**
Overall ADCC	.948	.906-.993	0.025*	.981	.960-1.003	0.094
A32-like ADCC	1.051	1.003-1.101	0.039*	1.033	.996-1.072	0.083
C11-like ADCC	1.014	.959-1.073	0.63	1.068	.990-1.153	0.088
Total cluster A-specific ADCC	1.031	1.002-1.060	0.034*	1.043	1.002-1.086	0.042*
17b-LALA-mediated enhancement	1.008	.998-1.018	0.13	1.015	1.000-1.031	0.049*

Table S1. Association of CD4i antibody-like ADCC or ADCC enhancement with infant survival adjusted for maternal viral load

The association of CD4i epitope-specific ADCC (A32-like ADCC, C11-like ADCC, or total cluster A-specific ADCC (sum of A32-like ADCC + C11-like ADCC)) and 17b-LALA-mediated enhancement of plasma ADCC with risk of infected infant mortality was measured using a Cox proportional hazards model adjusted for maternal plasma viral load. Adjusted hazard ratios (HR), 95% confidence intervals (CI), and p-values are shown for infant samples (passively-acquired ADCC, left, N=20) and maternal samples (maternal ADCC, right, N=21). Statistical significance was defined as $p<0{\cdot}05$ (*). Data from individual biological replicates from one maternal sample and one infant sample that were below the limit of detection were excluded from the analysis as described in the Materials and Methods.