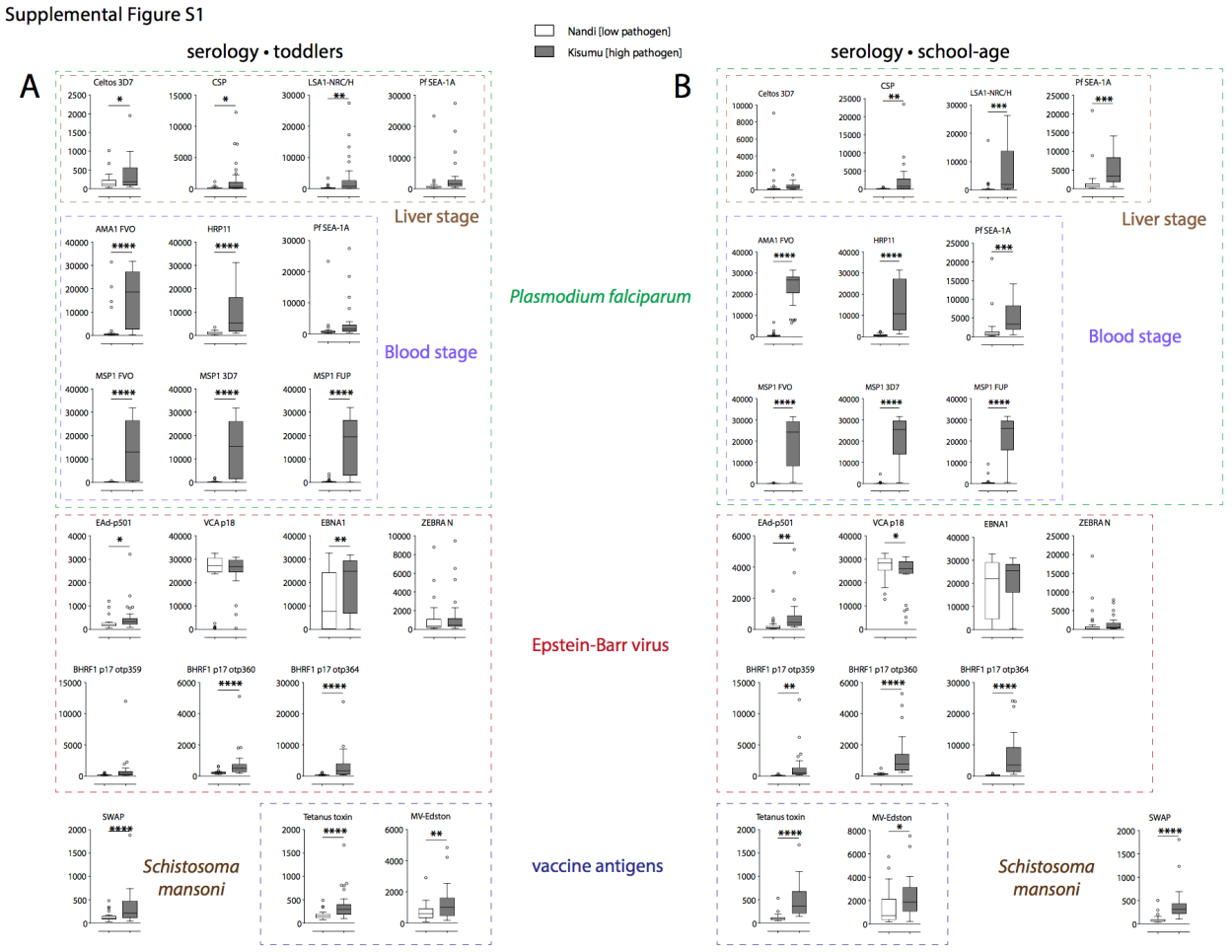


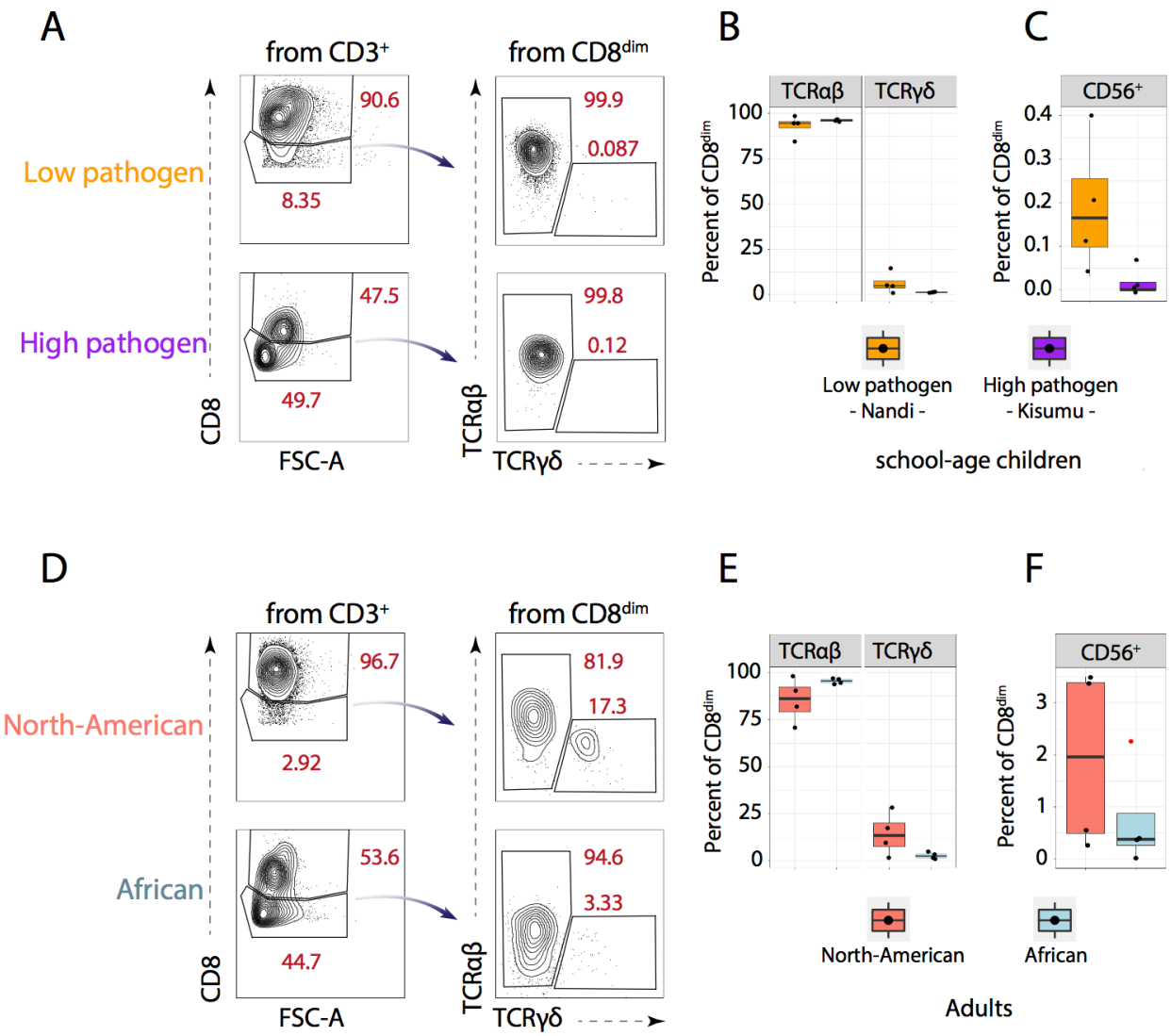
Supplemental Figure S1

Children from Nandi (low pathogen burden area) and Kisumu (high pathogen burden area) have significantly different pathogen-specific serological profiles.

Serum antibody titers for Plasmodium falciparum (Pf) malaria, EBV, schistosomiasis, were measured at a 4 year interval (toddlers to school-age) by suspension bead-based multiplex assay. Antibodies to vaccine antigens, i.e. measles and Tetanus toxoid were measured as controls. Nandi (low pathogen), n = 33; Kisumu (high pathogen), n = 31. Antibody titers (IgG) specific for Pf (HRP1, MSP1-FVO, CSP), Measles virus (Edmonston vaccine strain), Clostridium tetani (Tetanus), Schistosoma mansoni worm antigen protein (SWAP) and EBV

(EAD, ZEBRA, VCA, EBNA1) were measured using multiplex conjugated-bead suspension assay. Data on the boxplot (median and 95% IQR) displays the relative amount of antibody titers in toddlers [a] and school-age children [b] from Nandi (white bar) and Kisumu (grey bar). While open circles represent outliers, computed two-tailed unpaired t-test with Welch's correction p-values are displayed on each graph (* $P < 0.05$, *** $P < 0.001$, **** $P < 0.0001$).

Supplemental Figure S2



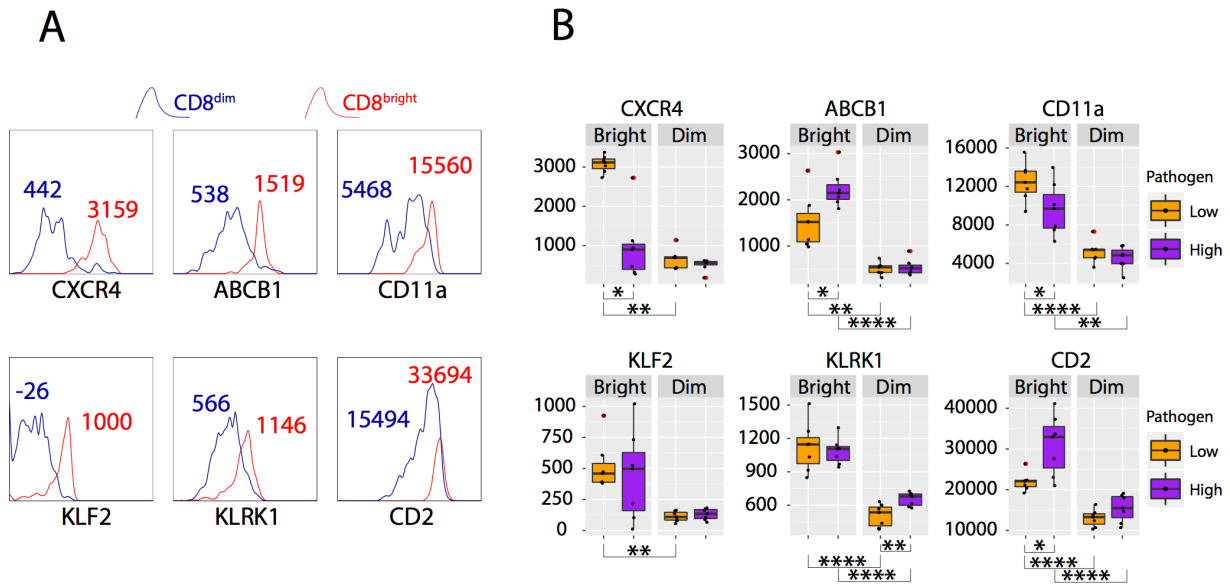
Supplemental Figure S2

CD3⁺ CD8^{dim} T cells are predominantly TCRαβ and not TCRγδ T cells

Peripheral blood mononuclear cells (PBMCs) were stained with fluorescently labeled antibodies and analyzed with a multiparameter flow cytometer. (**A**) Representative bivariate plot displaying the gating strategy for CD3⁺ CD8^{dim} T cells from school-age children living in low pathogen (n = 4) and high pathogen (n = 4) burden areas. (**B**) Boxplot (median + 95%

IQR) displaying cumulative proportions of $CD8^{dim}$ T cells expressing TCR$\alpha\beta$ and TCR$\gamma\delta$. (**C**) Boxplot (median + 95% IQR) showing cumulative proportions of $CD8^{dim}$ T cells expressing surface CD56. Data generated from one experiment. Black dots represent individual patients. (**D**) Representative bivariate of $CD3^{+}$ $CD8^{dim}$ T cells from North-American (n = 4) and African adults (n = 4) PBMCs. (**E**) Boxplot (median + 95% IQR) displaying cumulative proportions of $CD8^{dim}$ T cells expressing TCR$\alpha\beta$ and TCR$\gamma\delta$. (**F**) Boxplot (median + 95% IQR) displaying cumulative proportions of $CD8^{dim}$ T cells expressing surface CD56. Black dots represent individual patients. Outliers are depicted as red dots on the graph. Data generated from one experiment.

Supplemental Figure S3

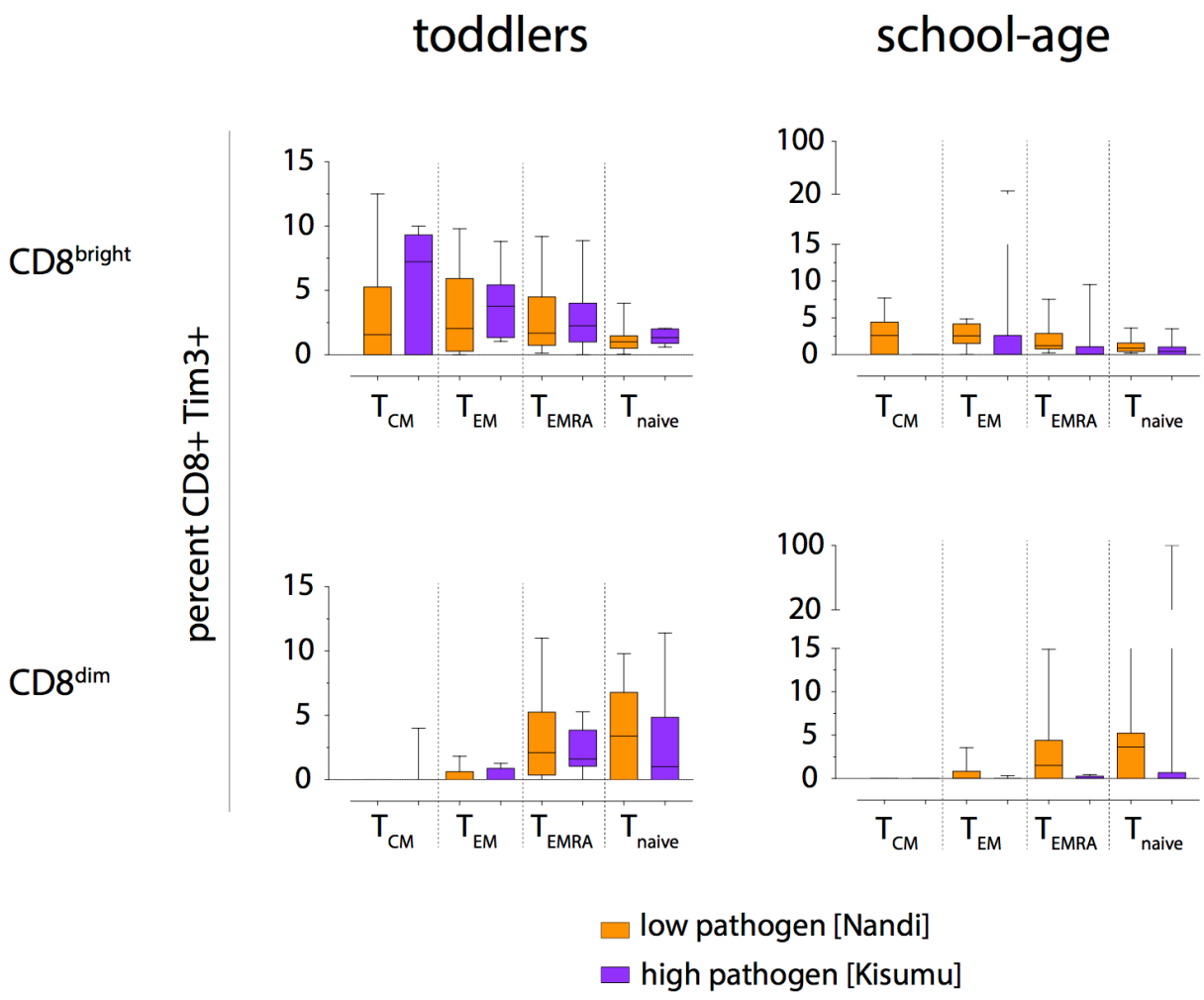


Supplemental Figure S3

Flow cytometry validation of differentially expressed targets identified via RNA-Seq between CD8^{bright} and CD8^{dim} TEM cells

Peripheral blood mononuclear cells (PBMCs) were from Nandi (n = 7) and Kisumu (n = 7) school-age children were stained with fluorescent antibodies and analyzed with a multiparameter flow cytometer. (**A**) Representative histograms of antibody staining on unstimulated T_{EM} CD8$^+$ T cells. (**D**) Boxplot (median and 95% IQR) of MFI from (**A**). Welch's two-tailed t test p-values are displayed (* P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001).

Supplemental Figure S4



Supplemental Figure S4

Children from Nandi and Kisumu have comparable proportions of CD8+ T cell subsets expressing Tim-3

Peripheral blood mononuclear cells (PBMCs) were stained with fluorescently labeled antibodies. Boxplot (median and 95% IQR) displaying the proportion of $CD8^{dim}$ and $CD8^{bright}$ T cell subsets expressing Tim-3 from toddlers and school-age children from Nandi (low pathogen burden, N = 14) and Kisumu (high pathogen burden, N = 15). There was no

statistical significance between CD8+ T cell subsets expressing Tim-3 based on pathogen burden after Welch's t-test correction however there was a trend for Tim-3 expression to be lost as children aged. Data cumulated from 9 independent experiments.