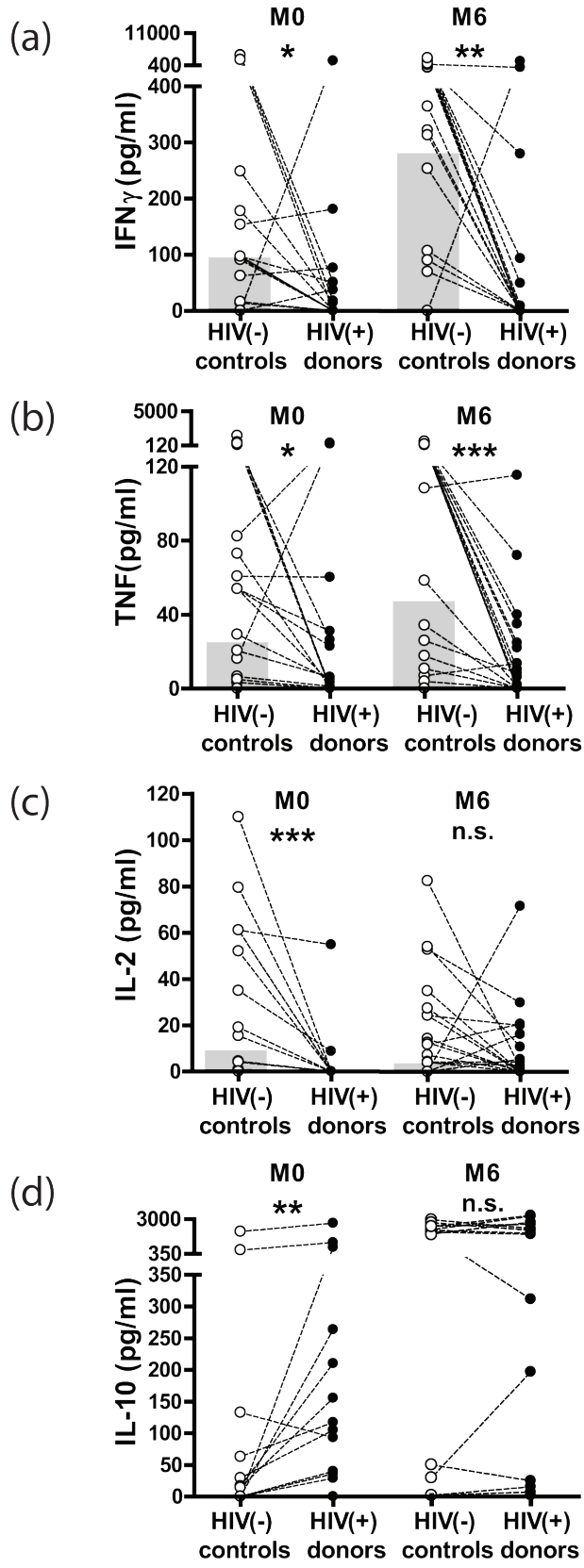
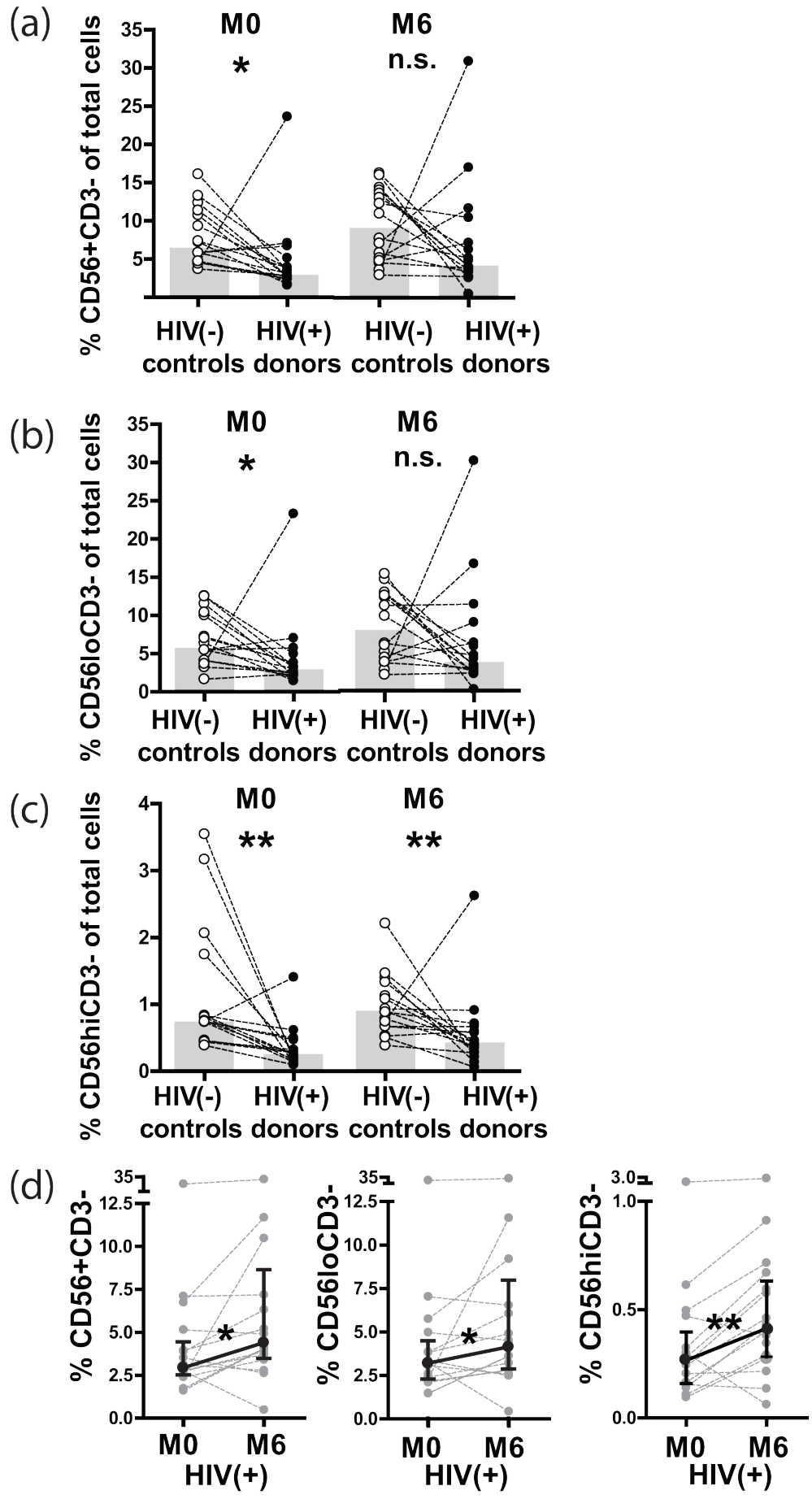
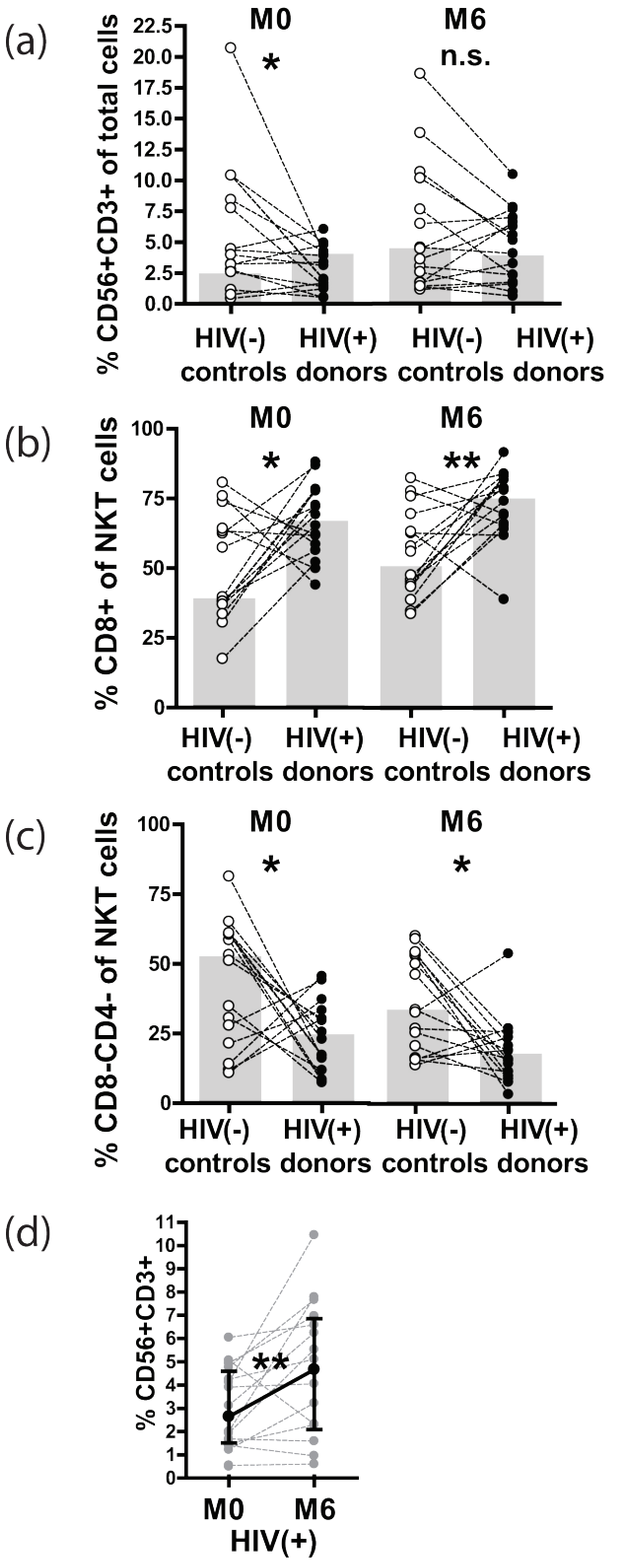


<u>Supplemental Fig. 1</u>: Malaria-specific cytokine responses are impaired in HIV(+) donors, and do not recover with cART. Cytokine levels were measured in PBMC culture supernatants at various time points for (a) IFNγ , (b) TNF, (c) IL-2, and (d) IL-10. Levels measured in wells containing uninfected RBC were subtracted from levels measured in wells with PEs to determine malaria-specific cytokine production (grey box represents median). HIV(+) donors (black circles) were matched to their HIV(-) controls (white circles). All statistical comparison by Wilcoxon matched pair test. * $p \leq 0.05$, ** $p \leq 0.01$, and *** $p \leq 0.001$, n = 24 pairs.

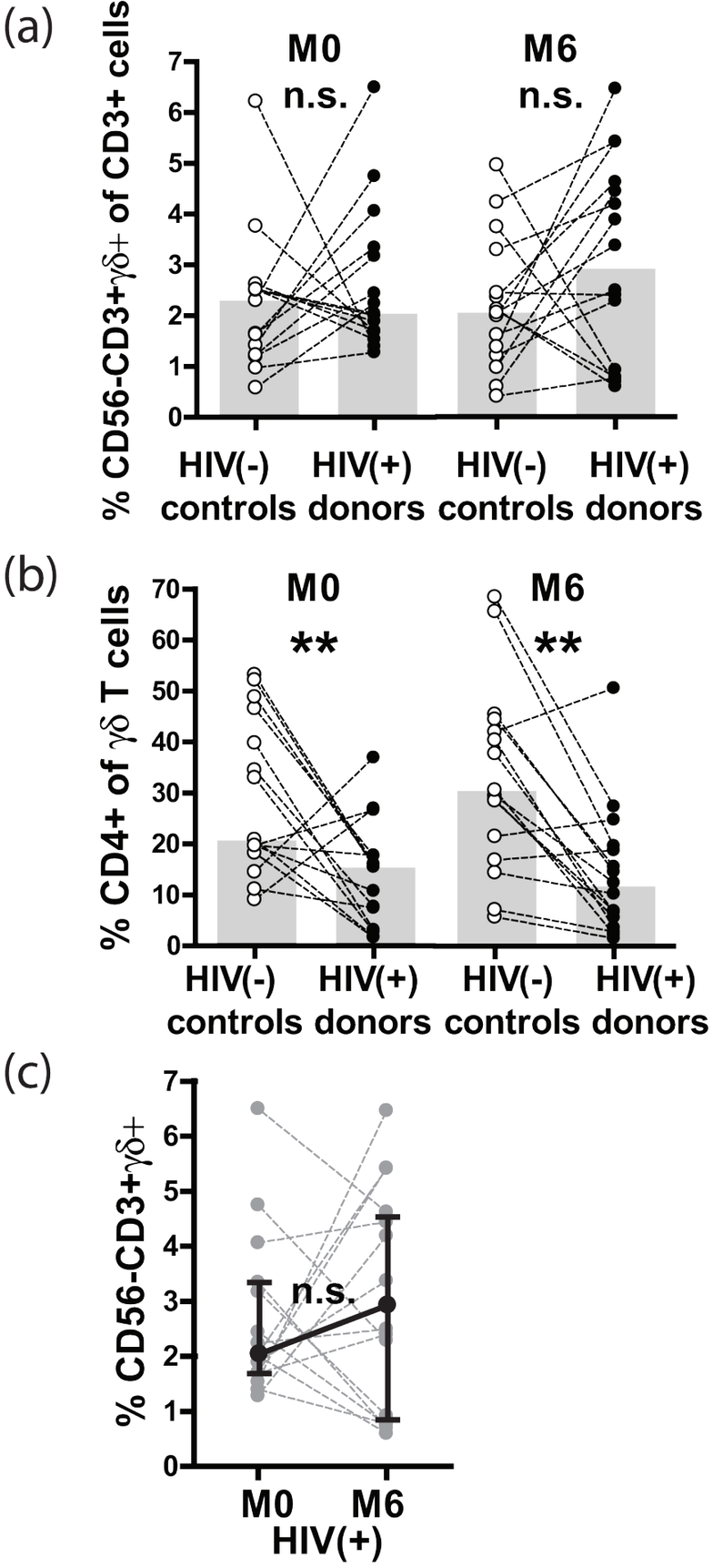


Supplemental Fig. 2: NK cells are lower in HIV(+) donors, but recover with cART.
NK cell subsets were identified in freshly isolated PBMCs from HIV(+) donors (black circles) and matched HIV(-) controls (white circles) by flow cytometry. Each pair of HIV(+) and HIV(-) donors are connected by a line. Analysis was performed prior to cART initiation (M0) and 6 months post-cART (M6). Grey bars represent median values. (a) NK cell (defined as percentage $CD14^{-}CD56^{+}CD3^{-}$ of total cells); (b) $CD56^{lo}$ NK cell (defined as percentage of $CD14^{-}CD56^{lo}CD3^{-}$ of total cells); (c) $CD56^{hi}$ NK cell (defined as percentage of $CD14^{-}CD56^{hi}CD3^{-}$ of total cells) percentages for HIV(+) and HIV(-) donors pre- and post-cART. (d) cART-induced changes in NK cell subsets from HIV(+) donors. All statistical comparisons by Wilcoxon matched pair test, n = 16. * $p \leq 0.05$, ** $p \leq 0.01$.



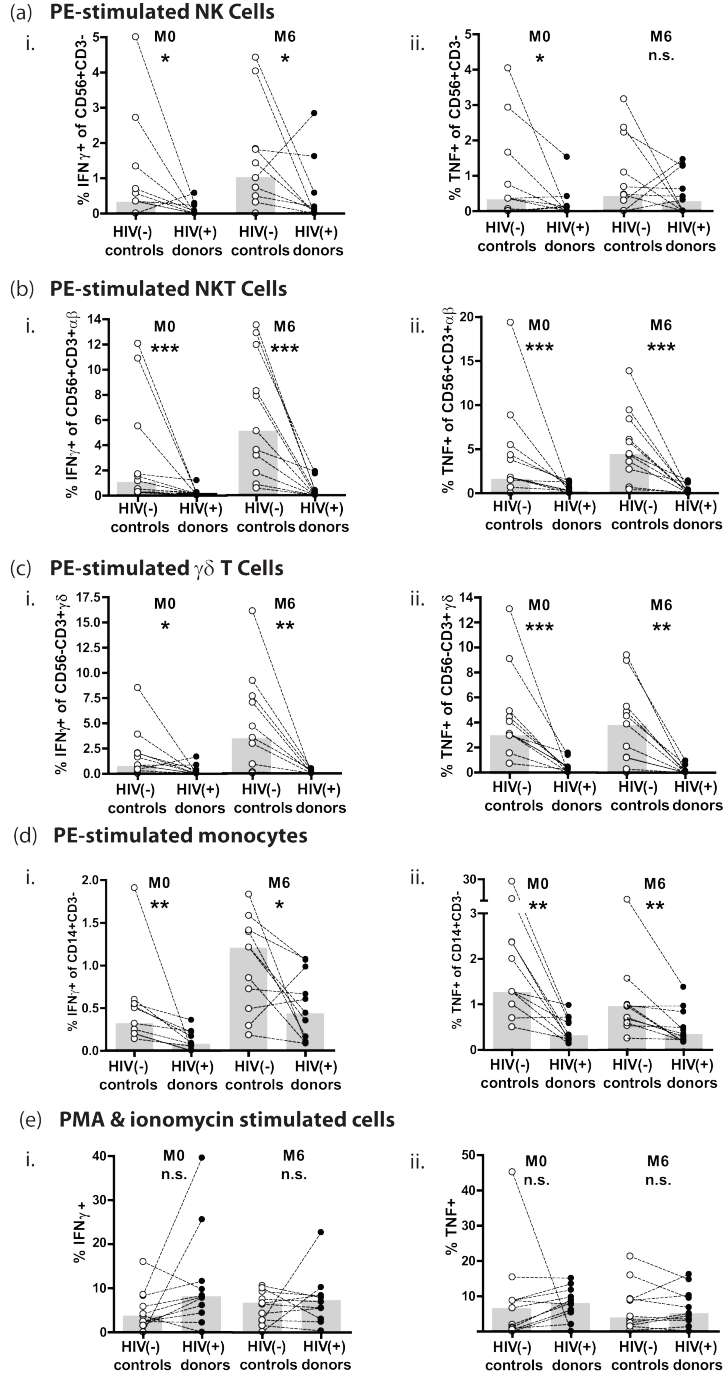
<u>Supplemental Fig. 3</u>: NKT subset differences between HIV(+) and HIV(-) donors persist despite cART.

NKT cell subsets were identified in freshly isolated PBMCs from HIV(+) donors (black circles) and matched HIV(-) controls (white circles) by flow cytometry. Each pair of HIV(+) and HIV(-) donors are connected by a line. Analysis was performed prior to cART initiation (M0) and 6 months post-cART (M6). Grey bars represent median values. (a) NKT cells (defined as the percentage $CD14^{-}CD3^{+}CD56^{+}$ of total cells); (b) CD8+ NKT cell (defined as the percentage CD8+ of NKT cells); and (c) $CD4^{-}CD8^{-}$ NKT cells (defined as percentage $CD4^{-}CD8^{-}$ of NKT cells) percentages for HIV(+) and HIV(-) donors pre- and post-cART. (d) cART-induced changes in NKT cells from HIV(+) donors. All statistical comparisons by Wilcoxon matched pair test, n = 16. * $p \leq 0.05$, ** $p \leq 0.01$.



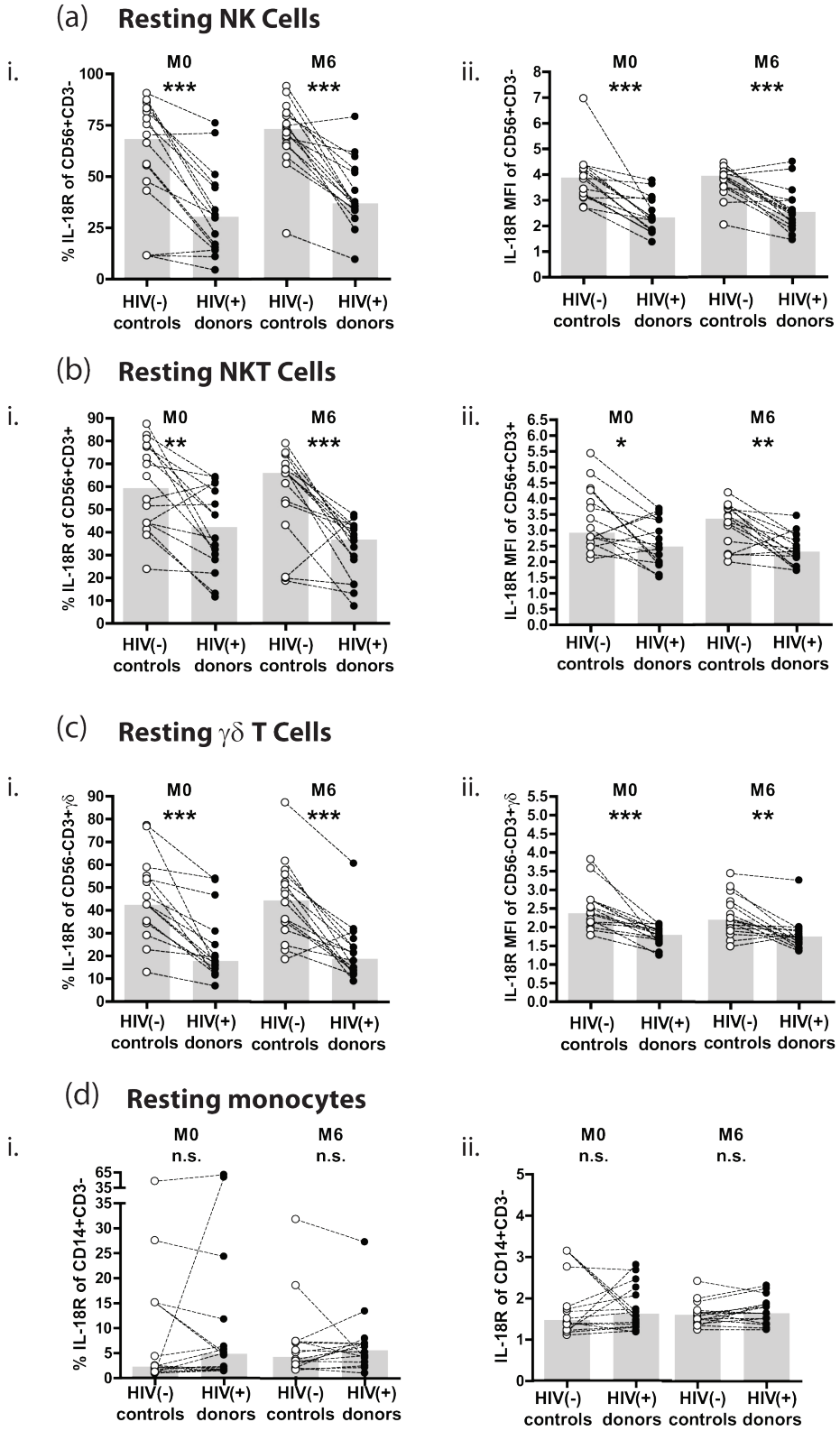
<u>Supplemental Fig. 4</u>: γδ T cells subset differences between HIV(+) and HIV(-) donors persist despite cART.

γδ cell T-cell subsets were identified in freshly isolated PBMCs from HIV(+) donors (black circles) and matched HIV(-) controls (white circles) by flow cytometry. Each pair of HIV(+) and HIV(-) donors are connected by a line. Analysis was performed prior to cART initiation (M0) and 6 months post-cART (M6). Grey bars represent median values. (a) γδ cell T-cells (defined as the percentage $CD14^{-}CD56^{-}CD3^{+}\gamma\delta^{+}$ of $CD14^{-}CD56^{-}CD3^{+}$ cells); and (b) $CD4^{+}$ γδ cell T-cells (defined as the percentage $CD4^{+}$ of γδ cell T-cell) for HIV(+) and HIV(-) donors pre- and post-cART. (c) cART-induced changes in γδ cell T-cells from HIV(+) donors. All statistical comparisons by Wilcoxon matched pair test, n = 15/16. ** $p \leq 0.01$.



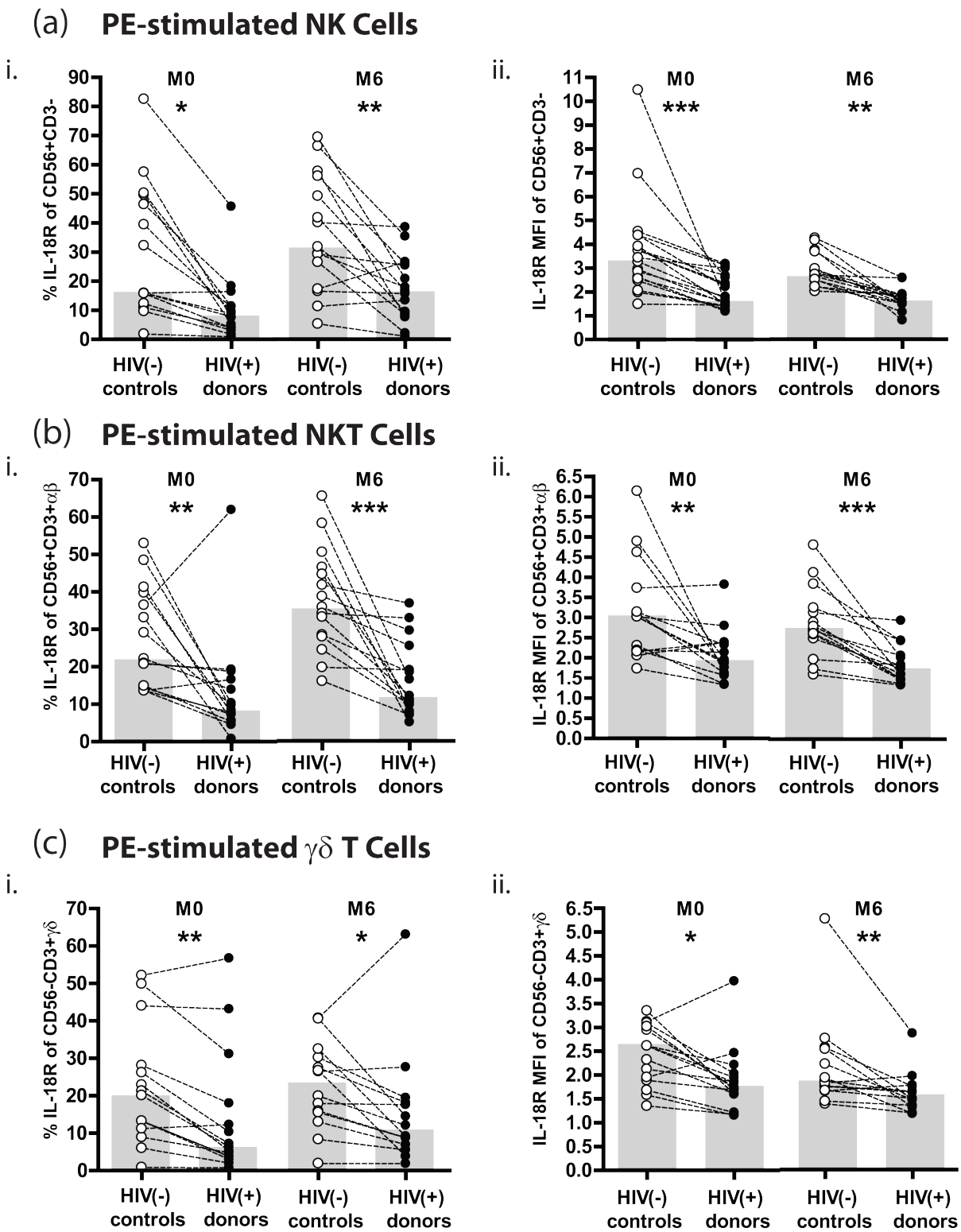
<u>Supplemental Fig. 5</u>: Innate immune cell malaria-specific cytokine production is impaired by HIV infection, despite cART.

PBMCs isolated from HIV(+) donors (black circles) and HIV(-) controls (white circles) were cultured in the presence of *P. falciparum* PEs for 72 hours prior to intracellular cytokine staining. Analysis was performed prior to cART initiation (M0) and 6 months post-cART (M6). Grey bars represent median values. *P. falciparum* PE-induced $IFN\gamma^+$ (i) and TNF^+ (ii) cells within the: (a) NK ($CD14^-CD3^-CD56^+$) subset (n = 11 pairs); (b) NKT ($CD14^-CD56^+CD3^+$) subset (n = 11 pairs); (c) γδ T-cell ($CD14^-CD56^-CD3^+\gamma\delta$) subset (n = 11 pairs); and (d) monocyte ($CD3^-CD14^+$) subset (n = 11 pairs) are shown for HIV(+) donors compared to HIV(-) controls pre- and post-cART. Levels of $IFN\gamma^+$ and TNF^+ cells measured in wells containing uninfected RBC were subtracted from levels measured in wells with PEs to determine malaria-specific cytokine producing cells. (e) PBMC isolated from HIV(+) donors and HIV(-) controls were cultured in the presence of PMA and ionomycin for 72 hours prior to intracellular cytokine staining. Levels (n = 11 pairs) measured in wells containing media alone were subtracted from levels measured in wells with PMA and ionomycin, to determine the cells responding to stimulus. The percentage of $IFN\gamma^+$ (i) and TNF^+ (ii) lymphocytes are shown. All statistical comparisons by Wilcoxon matched pair test. * $p \leq 0.05$, ** $p \leq 0.01$, and *** $p \leq 0.001$.



<u>Supplemental Fig. 6:</u> IL-18R levels are lower on resting NK, NKT, γδ T-cells, and monocytes from HIV(+) donors, and are not restored with cART.

The percentage IL-18R^{+} (i) and IL-18R mean fluorescence index (MFI) (ii) for (a) NK (CD14^{-}CD3^{-}CD56^{+}); (b) NKT (CD14^{-}CD56^{+}CD3^{+}); (c) γδ T-cells (CD14^{-}CD56^{-}CD3^{+}γδ); and (d) monocytes (CD14^{-}CD3^{-}) are shown for freshly isolated PBMCs from HIV(+) donors (black circle) and HIV(-) controls (white circles) analysed by flow cytometry, prior to (M0) and post-cART (M6). Pairs of HIV(+) and HIV(-) donors are connected by lines. MFI was calculated as the mean fluorescence intensity ratio between the IL-18R stained sample and its FMO control. Median levels are in grey (n = 16 pairs). All statistical comparisons by Wilcoxon matched pair test. * $p \leq 0.05$, ** $p \leq 0.01$, and *** $p \leq 0.001$.



<u>Supplemental Fig. 7:</u> IL-18R levels are lower on PE-stimulated NK, NKT, and γδ T-cells from HIV(+) donors, and are not restored with cART.

The percentage IL-18R$^+$ (i) and IL-18R mean fluorescence index (MFI) (ii) for (a) NK (CD14$^-$CD3$^-$CD56$^+$); (b) NKT (CD14$^-$CD56$^+$CD3$^+$); and (c) γδ T-cells (CD14$^-$CD56$^-$CD3$^+$γδ) are shown for PE-stimulated PBMCs from HIV(+) donors (black circle) and HIV(-) controls (white circles) analysed by flow cytometry, prior to (M0) and post-cART (M6). Pairs of HIV(+) and HIV(-) donors are connected by lines. MFI was calculated as the mean fluorescence intensity ratio between the IL-18R stained sample and its FMO control. Levels (median levels are in grey, n = 14/15 pairs) measured in wells containing uninfected RBC were subtracted from levels measured in wells with PEs to determine malaria-specific levels. All statistical comparisons by Wilcoxon matched pair test. * $p \leq 0.05$, ** $p \leq 0.01$, and *** $p \leq 0.001$.