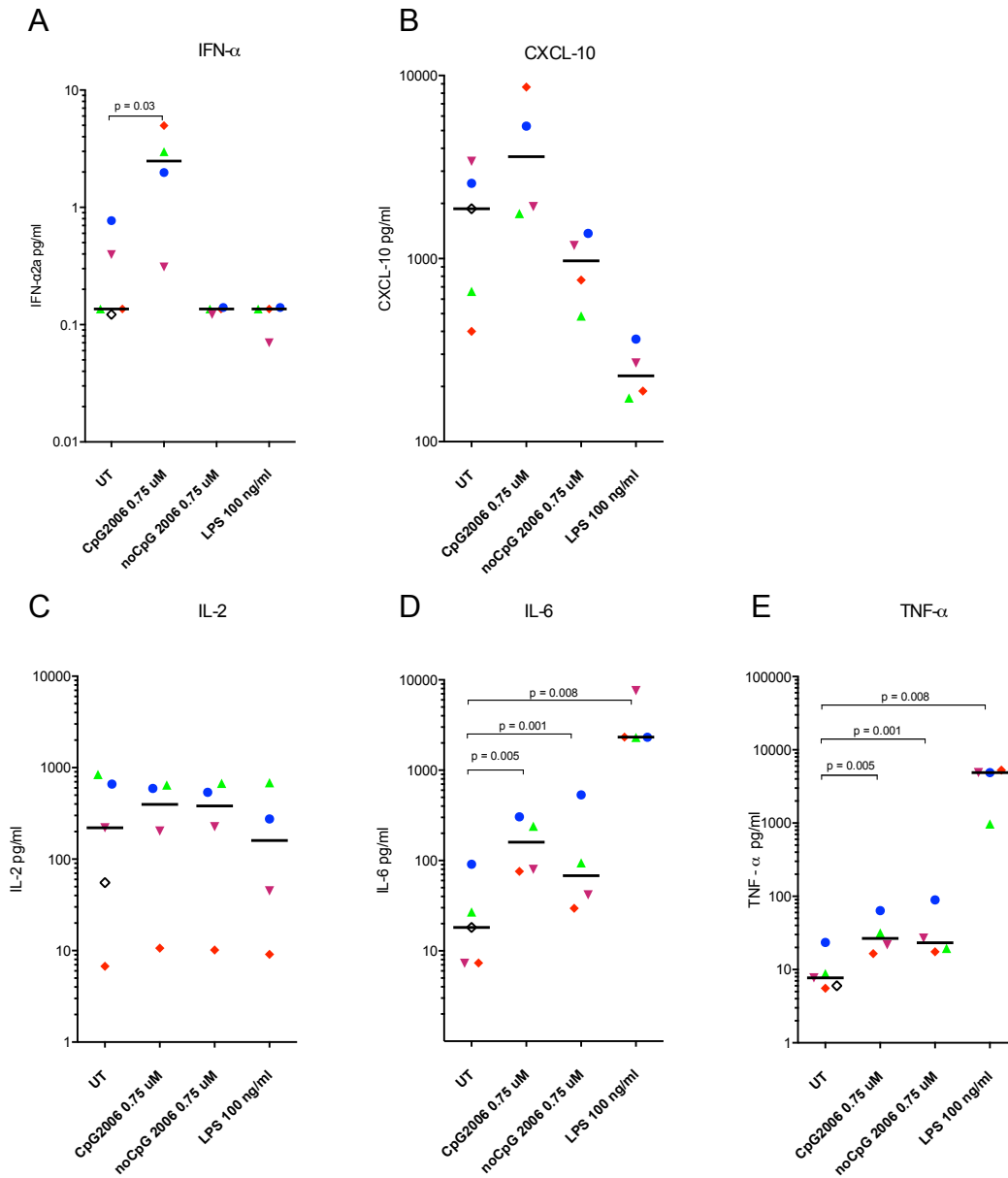


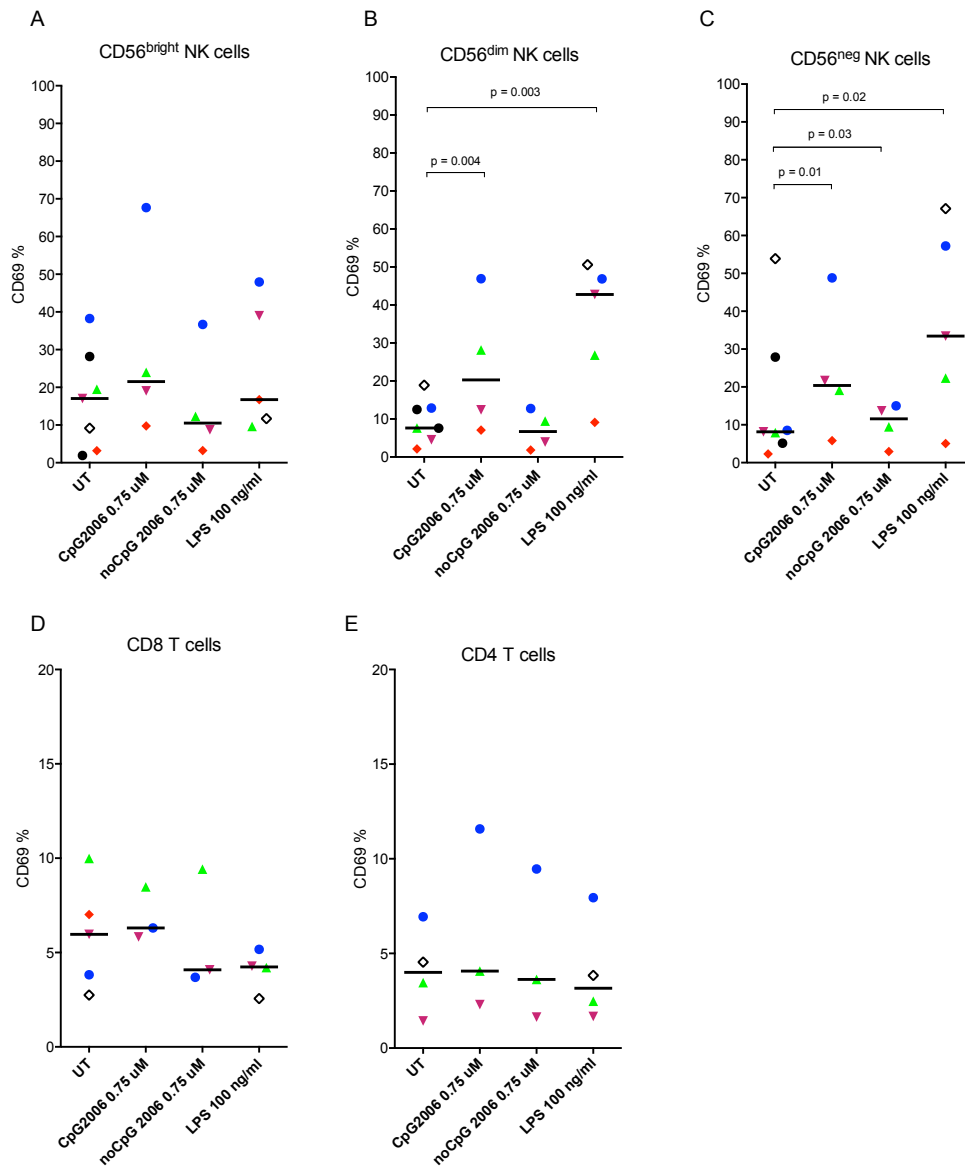
## Supplementary Figure 1



### Supplementary Figure 1: CpG2006 induces IFN- $\alpha$ , IL-2 and TNF- $\alpha$ .

PBMCs from ART-suppressed HIV-1 patients were stimulated for 48 hours with CpG2006 at indicated concentrations, noCG-CpG2006 as TLR9-specific negative control, or cRPMI as untreated control. Cytokine and chemokine levels were measured in culture supernatants. **(A+B)** CpG2006 induced a significant increase for IFN- $\alpha$ , but not for CXCL10. **(C-E)** No induction of IL-2 was observed, while IL-6 and TNF- $\alpha$  was significantly induced for LPS, CpG2006 as well as noCG-CPG2006, the latter showing a nonTLR9-induced effect of CpG2006. For comparative results for MGN1703 see Figure 1. Individual donors are displayed with same unique symbol as in Figure 1. Lines represent the median.

## Supplementary Figure 2

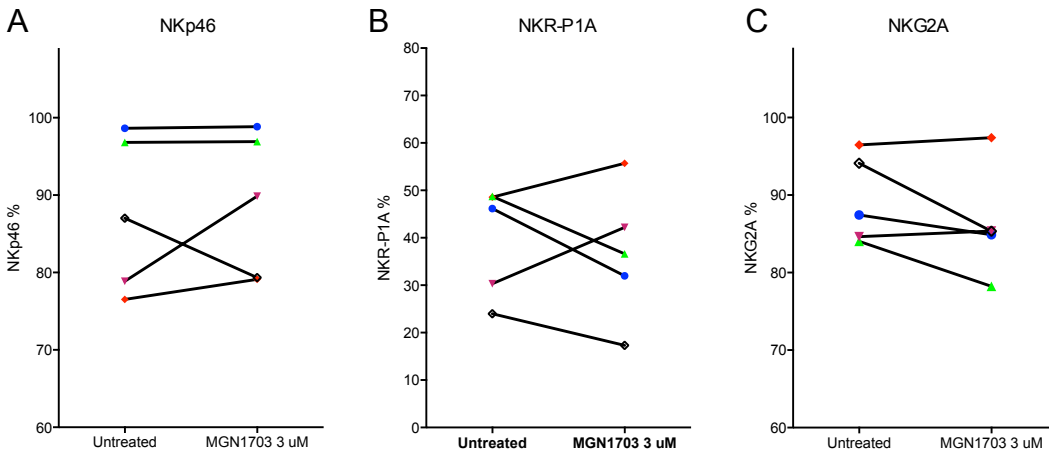


### Supplementary Figure 2: CpG2006 activates NK cells.

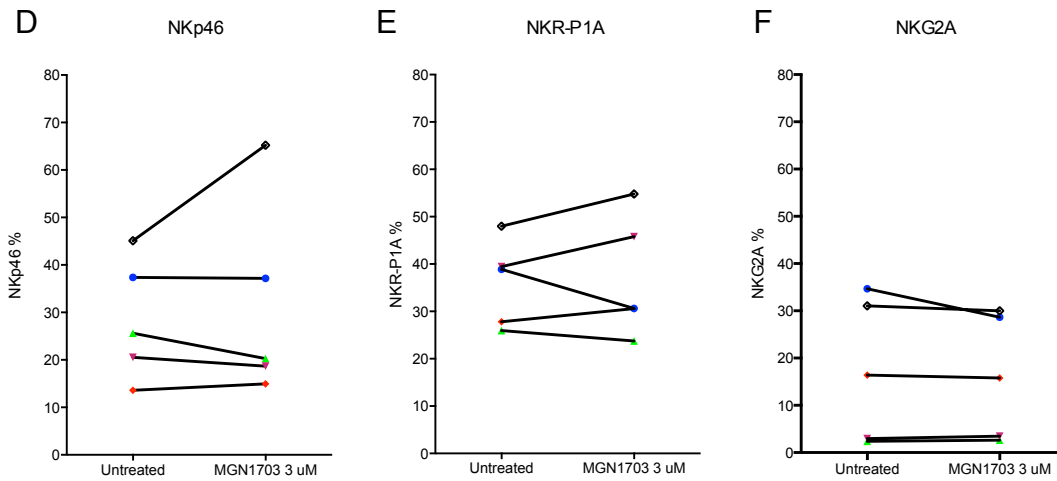
PBMCs from ART-suppressed HIV-1 patients were stimulated for 48 hours with CpG2006 at indicated concentrations, noCpG-CpG2006 as TLR9-specific control, LPS or cRPMI as untreated control. Cells were stained and assessed by flow cytometry. **(A-C)** The median percentage of CD69 positive CD56<sup>dim</sup> (CD56<sup>dim</sup>CD16<sup>+</sup>) NK cells and CD56<sup>neg</sup> (CD56<sup>neg</sup>CD16<sup>+</sup>) NK cells increased in response to CpG2006 and LPS. (for comparative results for MGN1703 see Fig. 2). **(D-E)** The numbers of activated CD8<sup>+</sup> T cells and CD4<sup>+</sup> T cells were unchanged. Individual donors are displayed with same unique symbol as in Figure 2. Lines represent the median.

### Supplementary Figure 3

CD56<sup>bright</sup> NK cells



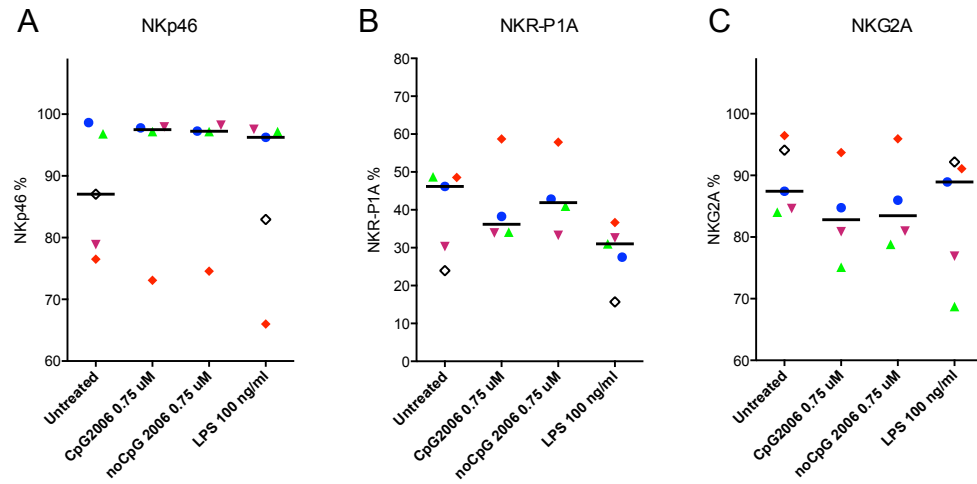
CD56<sup>neg</sup> NK cells



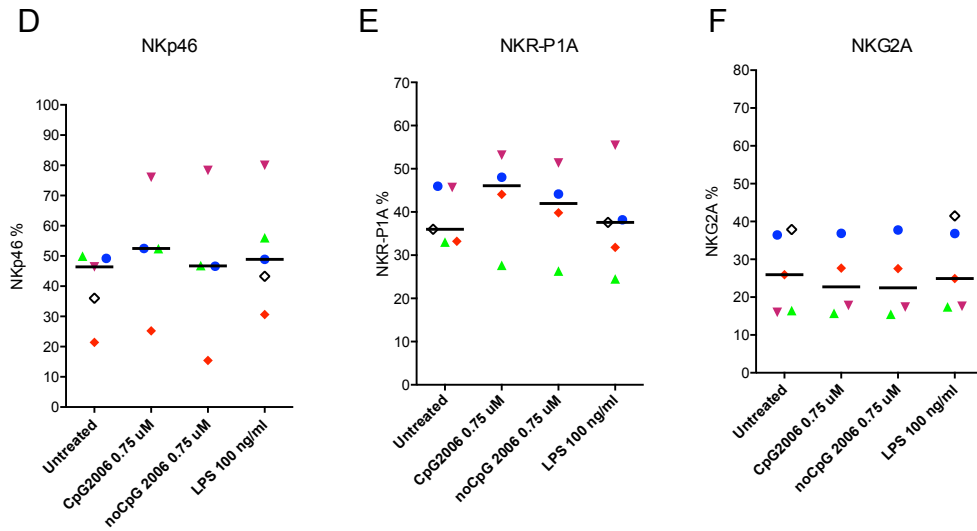
**Supplementary Figure 3: MGN1703 does not affect NK cell receptors on CD56<sup>bright</sup> and CD56<sup>neg</sup> NK cells.** PBMCs were incubated for 48 hours with MGN1703 or cRPMI as untreated control. Cells were stained and then assessed by flow cytometry. **(A-F)** MGN1703 stimulation did not affect NK cell receptors on either CD56<sup>bright</sup> and CD56<sup>neg</sup> NK cells. This is in contrast to the effect of MGN1703 on CD56<sup>dim</sup> NK cells (Figure 3). Individual donors are displayed with same unique symbols as in Figure 3. Lines represent the median.

## Supplementary Figure 4

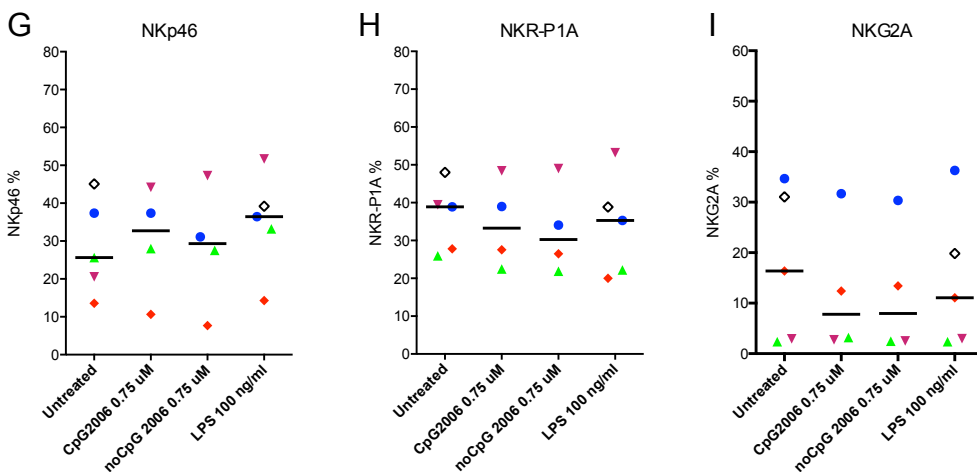
CD56<sup>bright</sup> NK cells



CD56<sup>dim</sup> NK cells



CD56<sup>neg</sup> NK cells

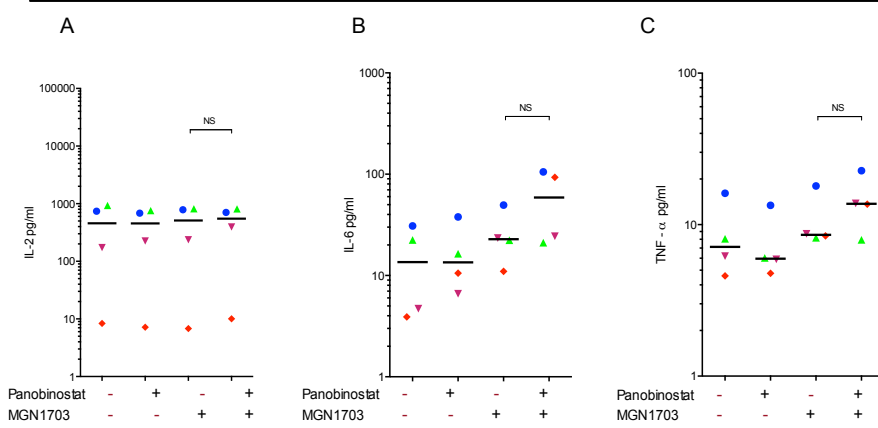


### Supplementary Figure 4: CpG2006 and LPS does not affect NK cell receptors on NK cells.

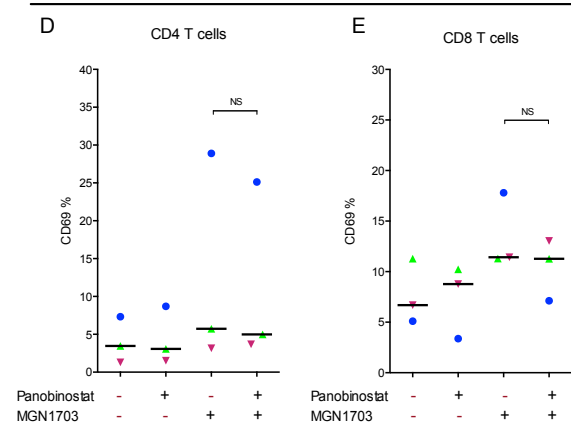
PBMCs from ART-suppressed HIV-1 patients were stimulated for 48 hours with CpG2006, noCG-CpG2006 as TLR9- specific control, LPS or cRPMI as untreated control. Cells were stained and assessed by flow cytometry. **(A-I)** CpG2006 or LPS stimulation did not affect NK cell receptors on neither CD56<sup>bright</sup>, CD56<sup>dim</sup> or CD56<sup>neg</sup> NK cells. This in contrast to the effect induced by MGN1703 on CD56<sup>dim</sup> NK cells (Fig. 3). Individual donors are displayed with same unique data points as in Fig. 3. Lines represent the median.

## Supplementary Figure 5

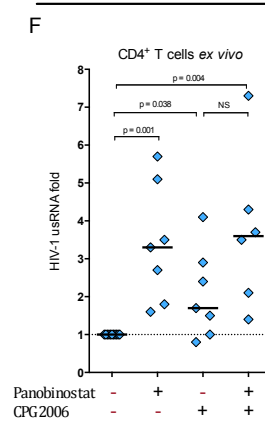
### Cytokines



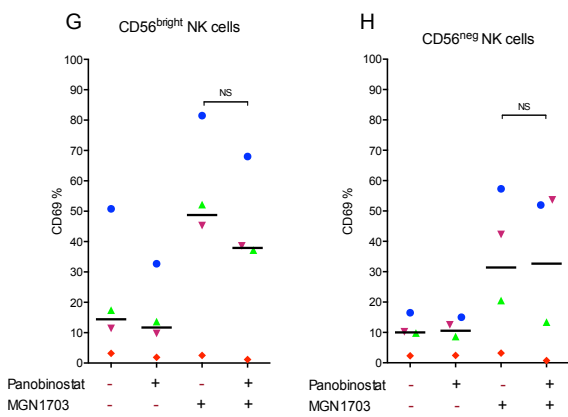
### T cell activation



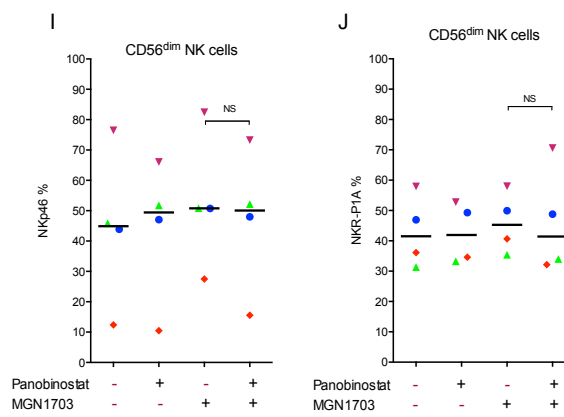
### HIV-1 usRNA *ex vivo*



### NK cell activation



### NK cell receptors



### Supplementary Figure 5: Panobinostat does not alter TLR9-induced functions.

PBMCs from ART-suppressed HIV-1 patients were stimulated for 16 hours with MGN1703 (3  $\mu$ M), CpG2006 (0.75  $\mu$ M), panobinostat (7.5 nM), or cRPMI as untreated control. Cells were stained and then assessed by flow cytometry. Cytokines were measured in culture supernatants. **(A-E and G-J)** Overall there was no significant difference between a TLR9 agonist alone versus co-administration with panobinostat. **(F)** CpG2006 significantly enhanced transcription of HIV-1 usRNA *ex vivo* (n=7) with levels comparable to MGN1703 (see Figure 5D), and did not inhibit viral transcription induced by panobinostat. Lines represent the median.