

### **Supplementary Figure 1**

**Gating strategy.** Panel A. The live, lymphocytic singlet population was used to gate on NK cells, which were defined as  $CD3^-$  and  $CD56^{+/-}CD16^{+/-}$ . Boolean gating was then used to determine the frequency of the possible combinations of  $IFN-\gamma$ ,  $TNF-\alpha$ ,  $CD107a$  and  $Z27$  expression on NK cells. Panel B shows flow cytometry plots using the isotype control for the  $Z27$  monoclonal antibody that was used to set the gate for  $KIR3DL1+$  NK cells (top row). An unstimulated control was used to set the gates for  $IFN-\gamma^+$ ,  $TNF-\alpha^+$  and  $CD107a^+$  NK cells (middle row). Panel C shows positive staining for  $IFN-\gamma$ ,  $TNF-\alpha$ ,  $CD107a$  and  $Z27$  in a K562 stimulated test sample (bottom row).

### **Supplementary Figure 2**

**Flow cytometry plots of the frequency of tri-functional NK cells from a representative \*h/\*y+B57 and Bw6 individuals.**

The frequency of tri-functional NK cells from representative \*h/\*y+B\*57 SP (upper panels) and Bw6 hmz SP (lower panels) are shown. In the left hand plots  $CD107a$  positive NK cells are gated on and in the right hand plots the following subsets of NK cells are identified;  $IFN-\gamma^-TNF-\alpha^-$  NK cells (Quadrant A),  $IFN-\gamma^+TNF-\alpha^-$  (Quadrant B),  $IFN-\gamma^+TNF-\alpha^+$  (Quadrant C),  $IFN-\gamma^-TNF-\alpha^+$  (Quadrant D). The frequency each NK cell subset is indicated in the quadrant with tri-functional cells shown in Quadrant C.

### **Supplementary Figure 3**

**Comparison of percentages of NK cells and NK subsets among HIV infected SP with different 3DL1/HLA-B combinations.**

SP carrying the 3DL1/HLA-B genotypes: \*h/\*y+B\*57, \*l/\*x+B\*57\*, h/\*y+Other-Bw4 and Bw6 hmz were compared for the percent of CD3<sup>-</sup>CD56<sup>+/-</sup>CD16<sup>+/-</sup> NK cells (A), CD56<sup>bright</sup> NK cells (B), CD56<sup>dim</sup> NK cells (C) and CD56<sup>-</sup>CD16<sup>+</sup> NK cells (D). Mann-Whitney *U* tests were used to assess the significance of between-group differences. P-values <0.05 are shown over the line connecting the two groups being compared.