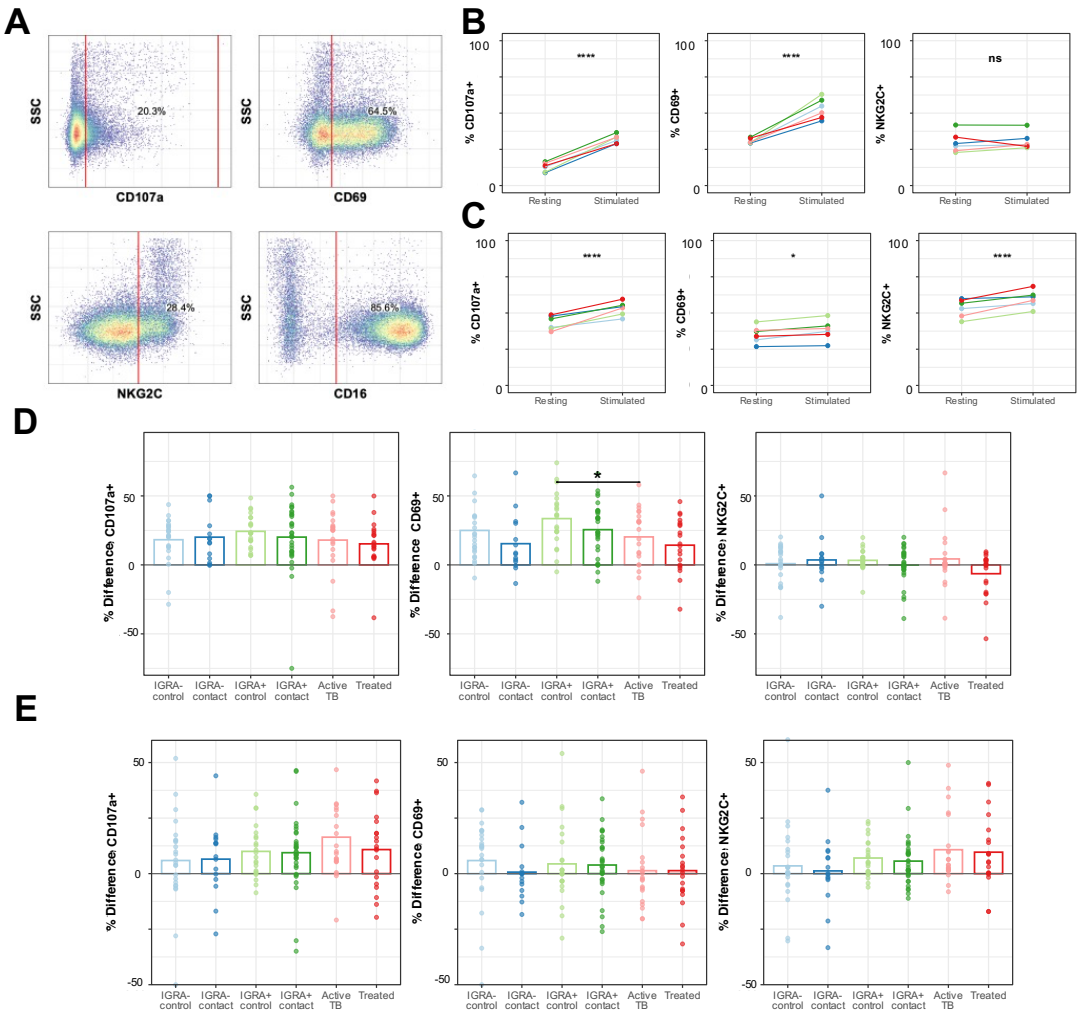

Fig. S1. CD56^{bright} and CD56^{-} NK cell response to K562 re-stimulation measured by CD69, CD107a, and NKG2C surface expression. (A) Representative flow plots of the percent positive gates for the markers CD69, CD107a, NKG2C, and CD16. **(B)** Overall results of activation assay for CD56^{bright} NK cells for each activation marker. Y-axis represents mean percent positive. P values calculated as a global paired Wilcoxon test including all clinical groups. Each clinical group is displayed separately indicated by line color. Same color legend as Figure 3. **(C)** Overall results of activation assay for CD56^{-} NK cells, as in panel B. **(D)** Percent difference (stimulated minus resting) of three activation markers in CD56^{bright} NK cells compared between clinical groups. Brackets represent Wilcoxon tests with unadjusted p values. **(E)** Percent difference (stimulated minus resting) of three activation markers in CD56^{-} NK cells compared between clinical group. Brackets represent Wilcoxon tests with unadjusted p values. *p ≤ 0.05, ****p ≤ 0.0001.

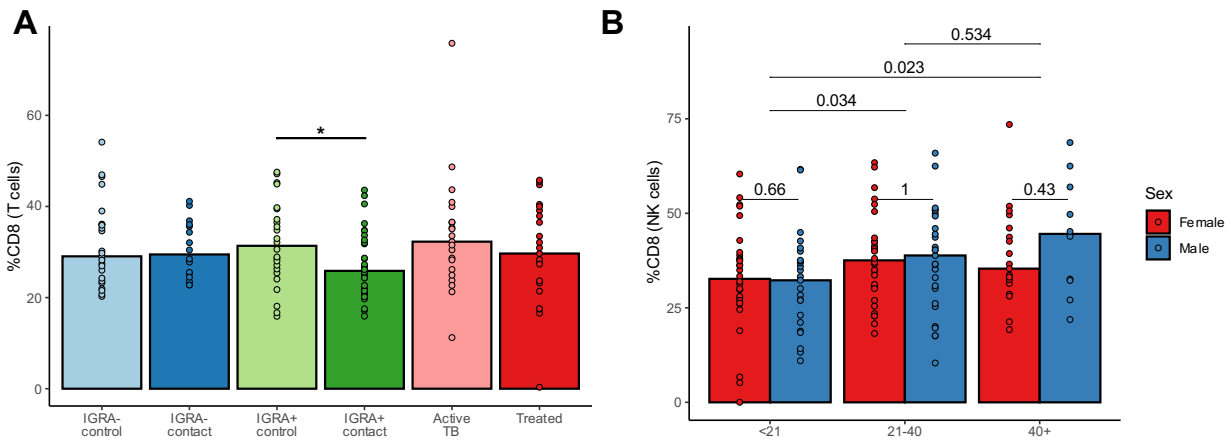

Fig. S2. CD8α expression in T cells and NK cells stratified by age and sex. (A) Bar graph demonstrating frequency of T cells that are CD8α positive compared between clinical groups. Brackets represent Wilcoxon tests. **(B)** Bar graph demonstrating frequency of $CD8\alpha^{+}$ NK cells stratified by age and sex. Color represents sex, with three age ranges displayed. Brackets represent Wilcoxon tests. *$p \leq 0.05$.

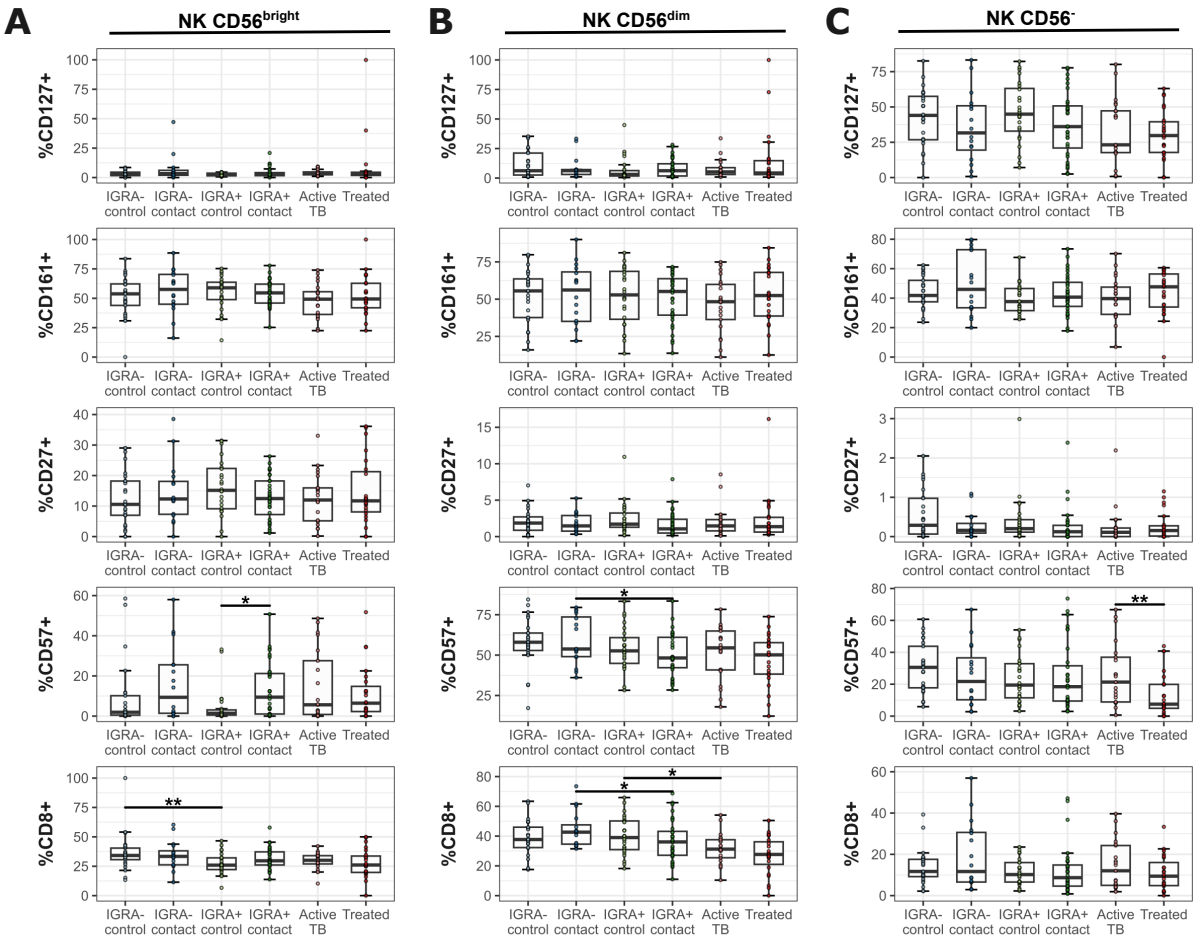

Fig. S3. Baseline surface expression for potential memory markers among NK cell subsets in ex vivo stained samples. Percent positive of five putative memory markers in **(A)** $CD56^{bright}$, **(B)** $CD56^{dim}$, and **(C)** $CD56^{-}$ NK cells. Brackets represent Wilcoxon tests with unadjusted p values. *$p \leq 0.05$, **$p \leq 0.01$.

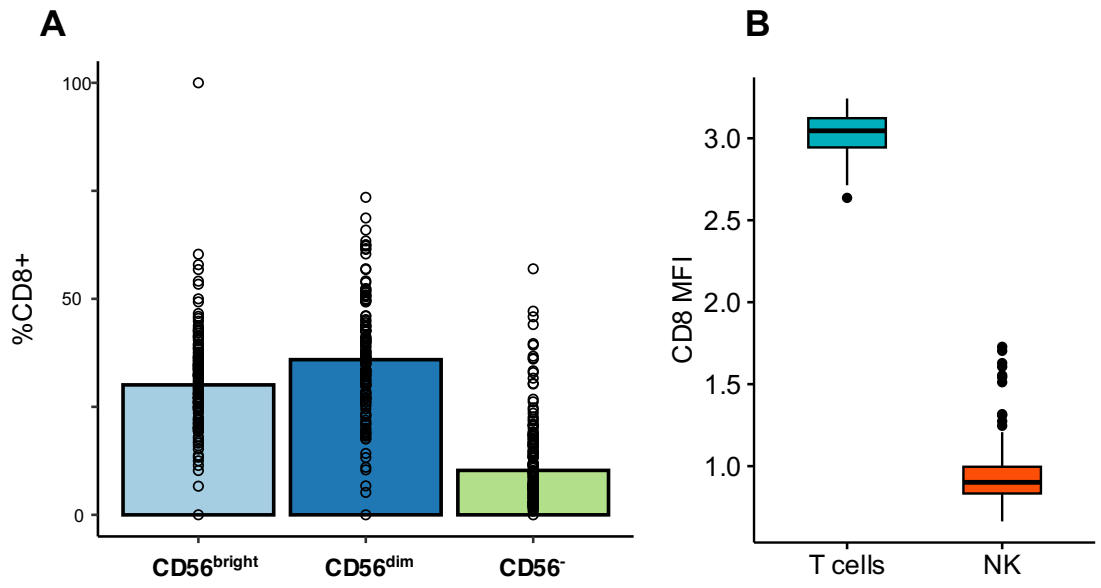

Fig. S4. Expression of CD8α among three NK cell subsets: CD56^{bright}, CD56^{dim}, and CD56^{-}. (A) Median CD8α frequency across CD56-stratified NK cell subsets. (**B)** Boxplot of MFI values between CD8α^{+} NK cells versus CD8α^{+} T cells.

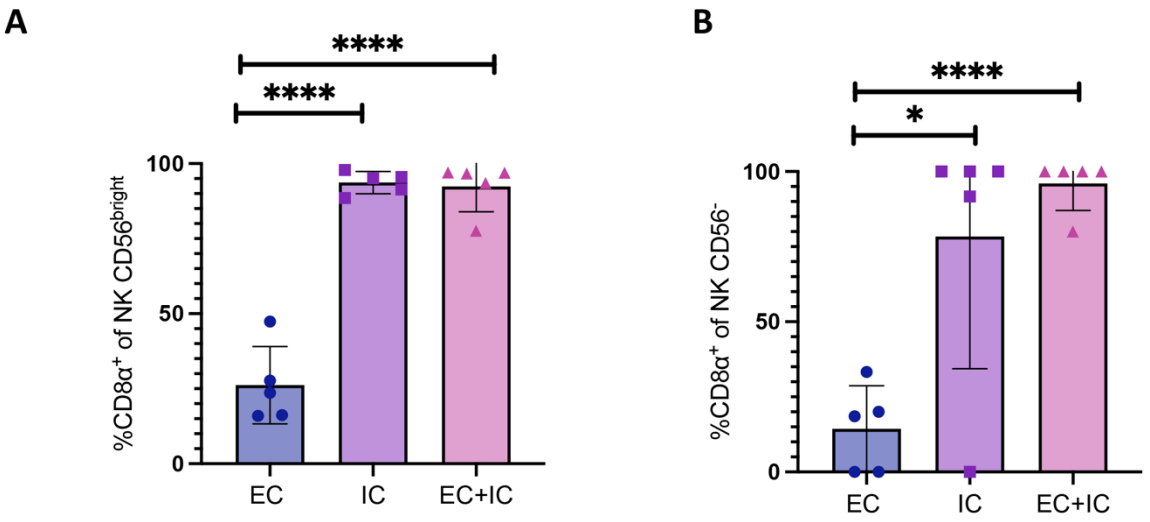

Fig. S5. Ubiquitous intracellular CD8α expression among CD56^{-} and CD56^{bright} NK cells. Percentage of CD8α^{+} cells in **(A)** CD56^{bright} and **(B)** CD56^{-} NK cells using extracellular antibody staining, intracellular antibody staining, and both combined. Brackets represent unpaired t tests. EC (**e**xtra**c**ellular/surface), IC (**i**ntra**c**ellular), and EC + IC (both extracellular and intracellular). *p<0.05, ****p<0.0001.

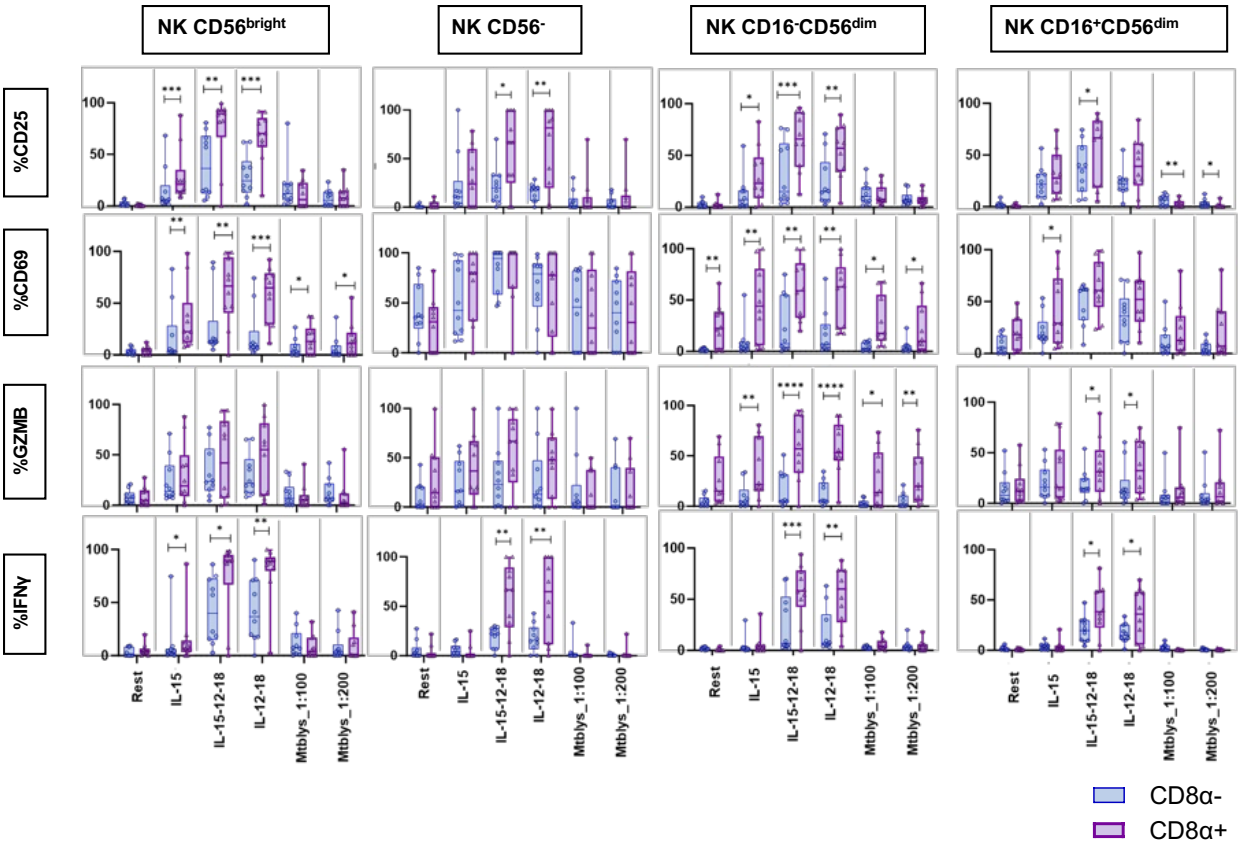

Fig. S6. Enhanced responsiveness of CD8α^{+} NK cell subsets after cytokine stimulation. NK cells were cultured for 15 hours in either complete media or supplemented with IL-15-Su, IL15-Su/12/18, IL-12/18, or MtbLys at dilutions of 1:100 and 1:200. Percent positive of CD25, CD69, granzyme B (GZMB) and Interferon gamma (IFNγ) in CD8α^{+} and CD8α^{-} CD56^{bright}, CD56^{-}, and CD16$^{-/+}$ CD56^{dim} NK cell populations measured by flow cytometry. *p ≤ 0.05, **p ≤0.01,***p ≤0.001 ****p ≤ 0.0001

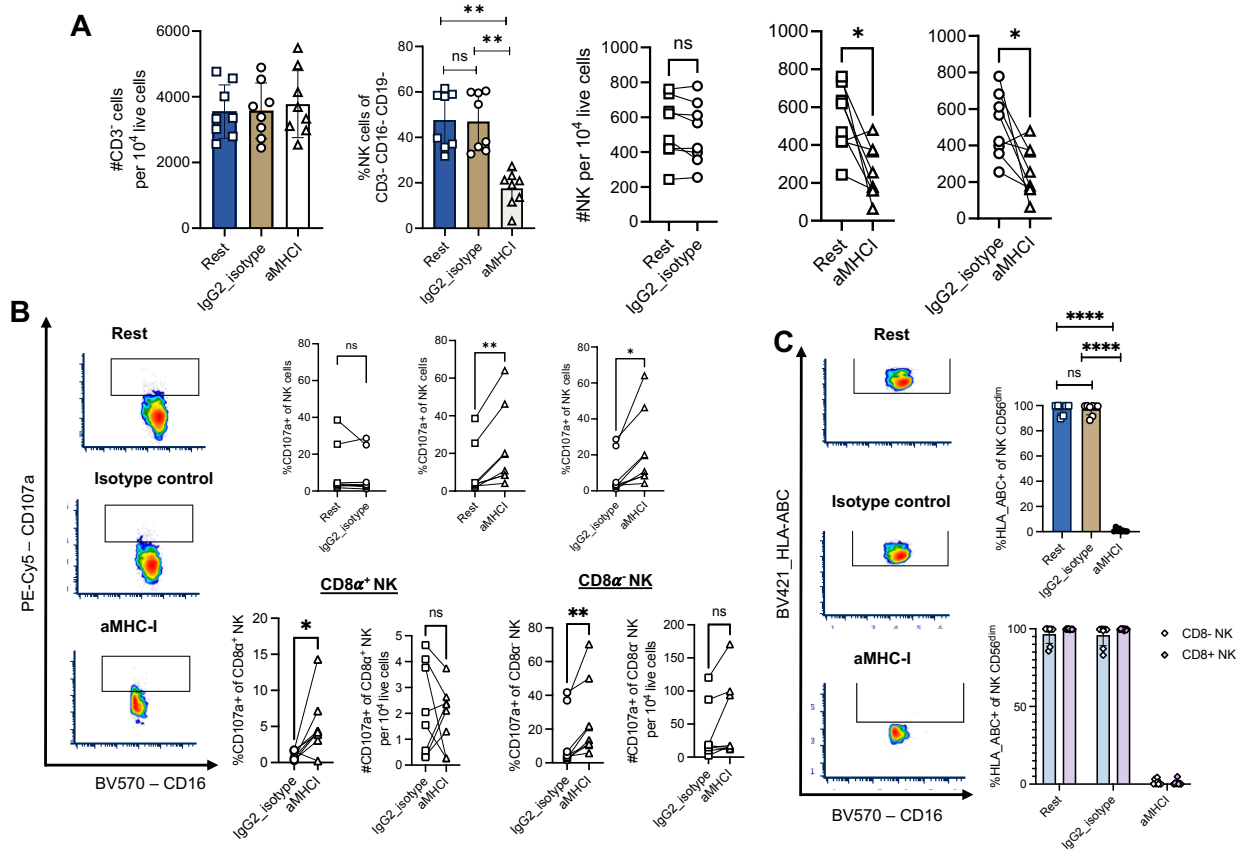

Fig. S7. MHC class I blockade depletes total NK cells and induces NK cell degranulation. **(A)** Normalized absolute count of $CD3^-$ compartment and $CD16^+CD56^{dim}$ NK cells after incubation with anti-MHC class I or IgG2 isotype control. **(B)** Frequency and normalized absolute counts of NK cells undergoing degranulation measured by CD107a staining after incubation with anti-MHC class I or IgG2 isotype control stratified by CD8α. **(C)** Frequency of HLA_ABC^+ NK cells after incubation with anti-MHC class I or IgG2 isotype control stratified by CD8α. Statistical significance was measured using unpaired t tests, with threshold of *p<0.05, **p<0.01, ****p<0.0001.

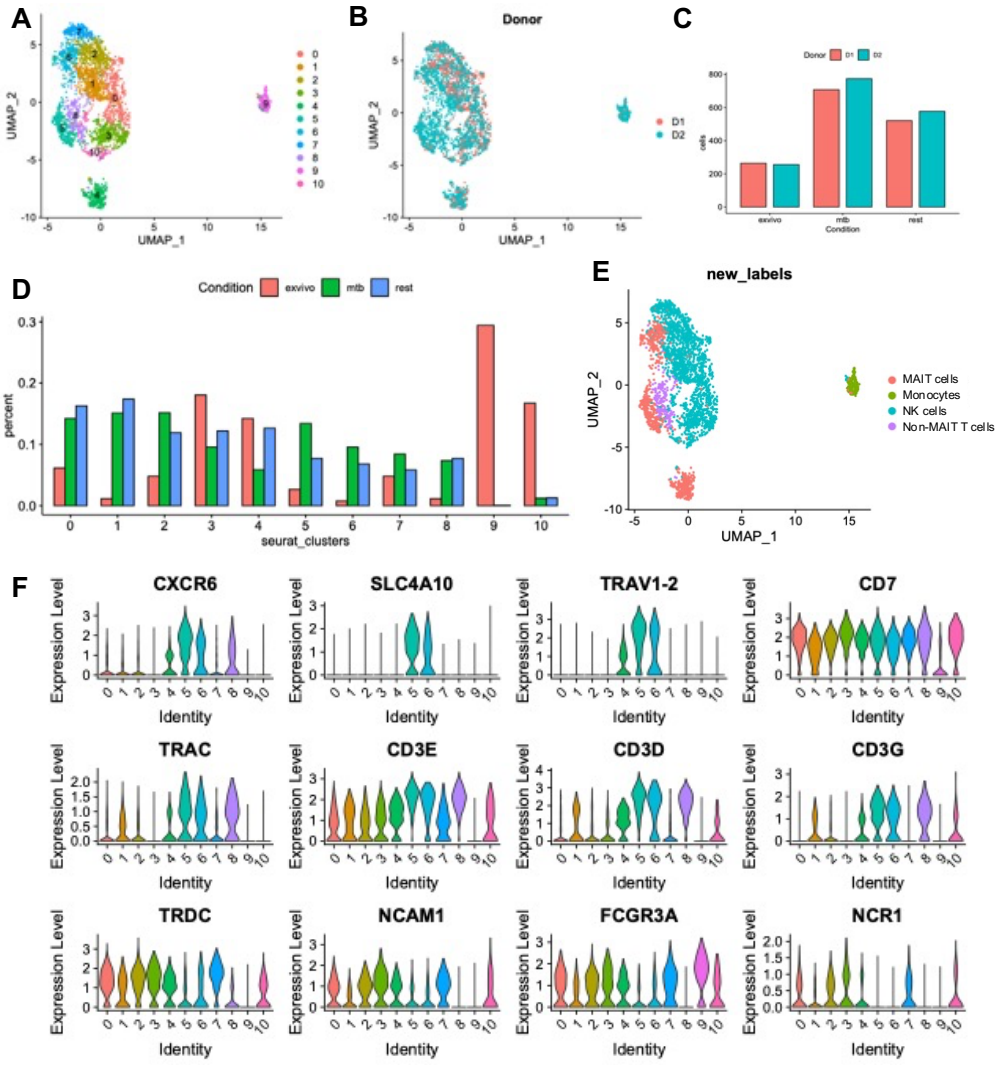

Fig. S8. CITE-seq clustering of sorted MAIT cells, iNKT, NK cells, and γδ T cells in three stimulation conditions. **(A)** UMAP representation of Louvain clustering output. **(B)** Cells labeled by donor origin. **(C)** Bar graph of total cells per donor and condition. **(D)** Bar graph of total number of cells per cluster separated by condition. **(E)** Final annotation of clusters after merging of similar clusters. **(F)** Expression of select markers comparing original cluster identities.

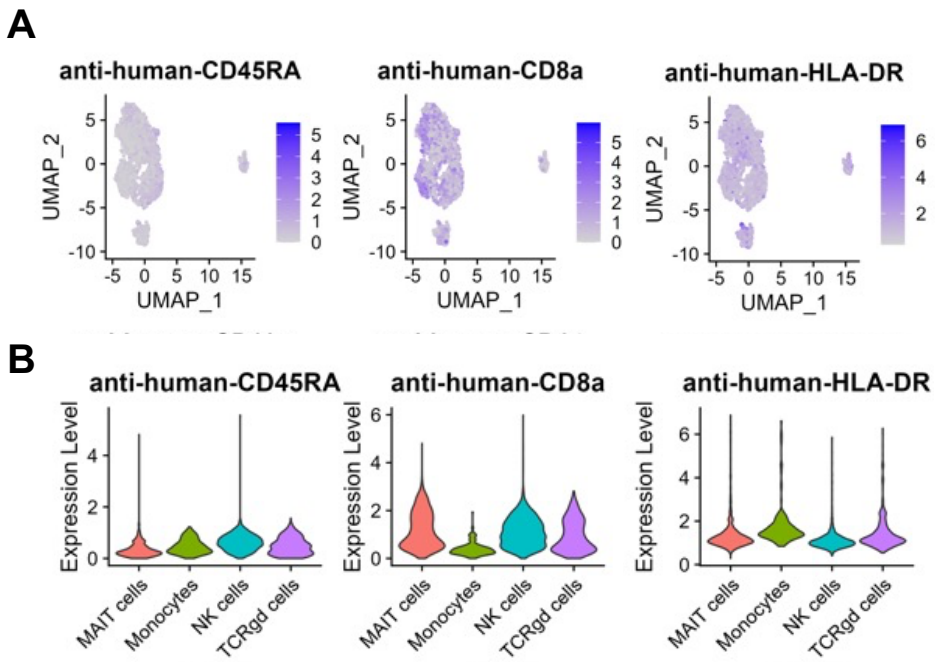

Fig. S9. CITE-seq of innate lymphocytes analyzed by surface barcode antibody detection in annotated clusters of MAIT cells, iNKT, NK cells, and γδ T cells. (A) UMAP representation of all cells colored by surface expression of antibody stated in the plot title. **(B)** Violin plot of the expression level of three selected markers in each cell subset after manual annotation.