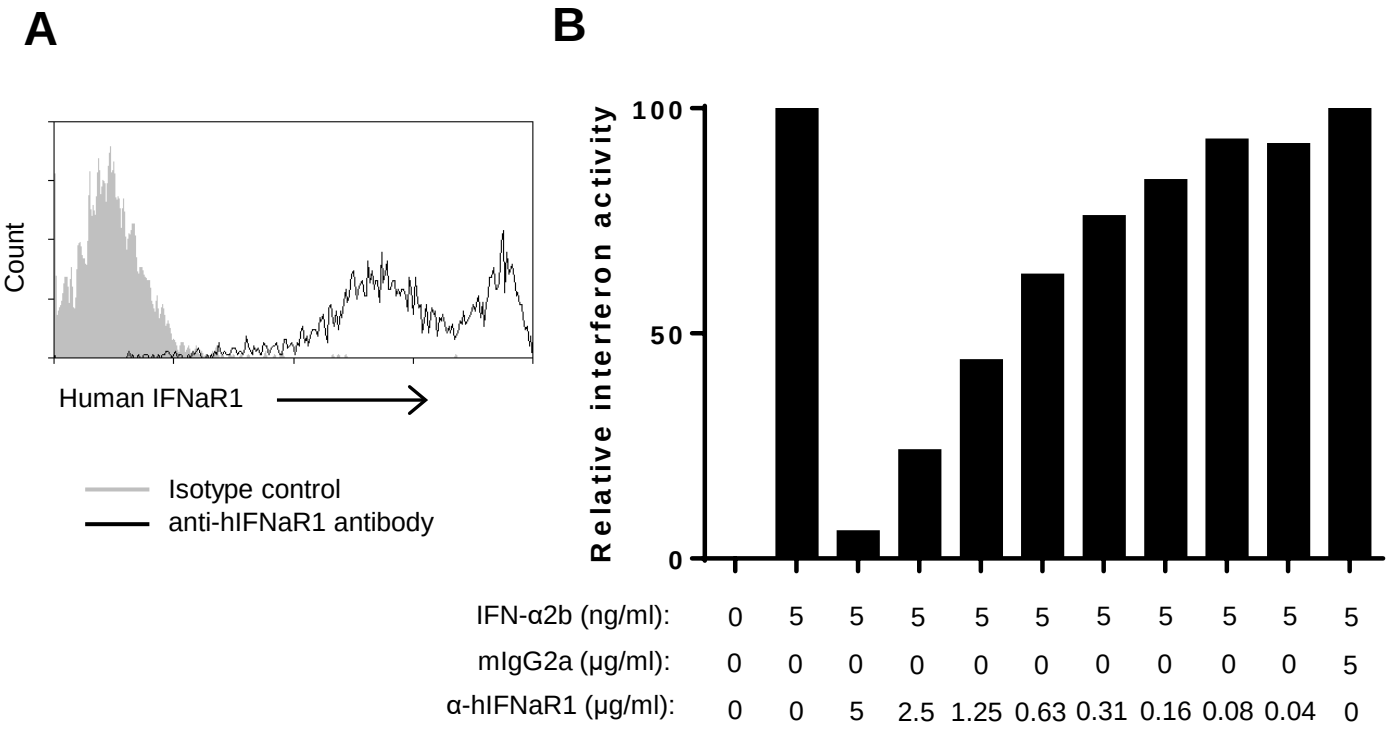
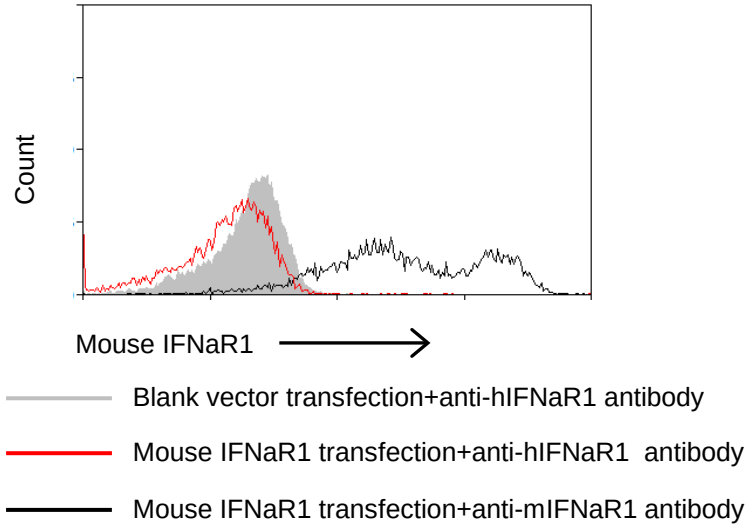


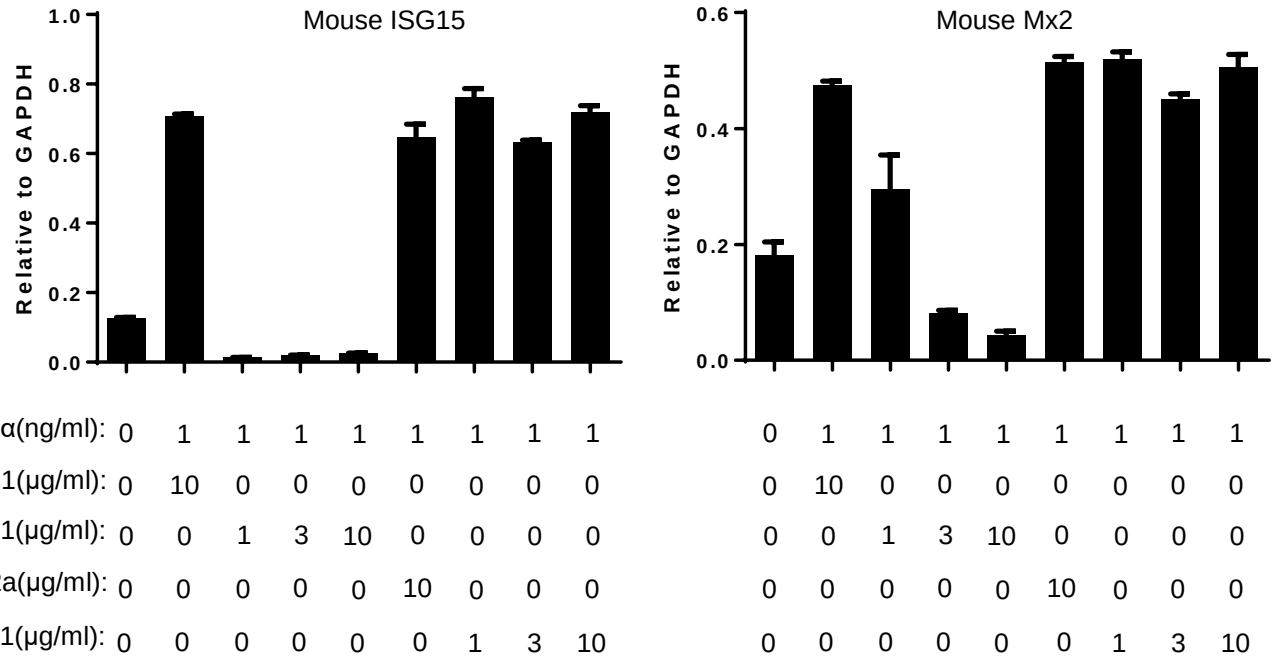
Supplementary Figure 1. The a-IFNaR1 antibody can bind human IFNaR1 and block type I interferon signaling. (A) Histogram show the binding of anti-human IFNaR1 antibody to 293T cells transfected with plasmid encoding human IFNaR1. mIgG2a was used as isotype control. (B) The IFN-I reporter cell line was stimulated with human IFN-a2b in the present of anti-human IFNaR1 or isotype control mIgG2a antibody. Data show IFN activity after anti-human IFNaR1 treatment relative to samples with IFN-α2a treatment only. The half maximal inhibitory concentration (IC50) is 1.04μg/ml. (C) Human PBMCs were pre-incubated with anti-human IFNaR1 antibody for 1 hour and then stimulated with human IFNα2b for 5 hours. Data show the relative expression of human ISG15 and Mx2 detected by quantitative RT-PCR.

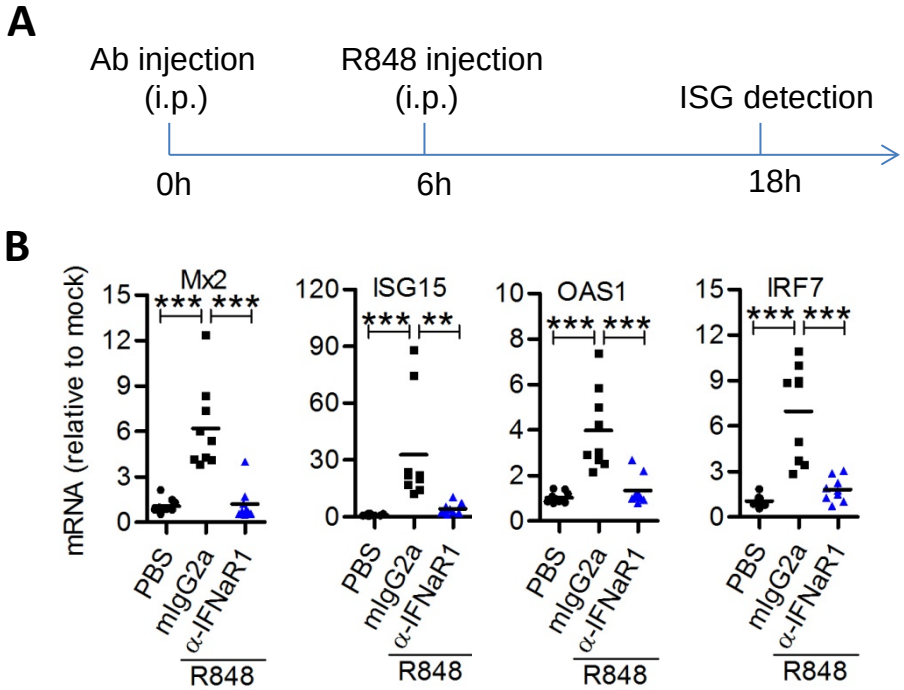
A



Supplementary Figure 2. The anti-human IFNaR1 antibody do not bind to mouse IFNaR1 or block IFN-a mediated signaling in mouse cells. (A)293T cells were transfected with blank plasmid and plasmid encoding mouse IFNaR1, then incubated with anti-human IFNaR1 antibodies to test the binding of the anti-human IFNaR1 antibody to mouse IFNaR1. anti-mouse IFNaR1 antibody was used as positive control. (B) Splenocytes from mouse were pre-incubated with anti-human IFNaR1 antibody or anti-mouse IFNaR1 antibody for 1 hour and then stimulated with mouse IFNα for 4 hours. Data show the relative expression of mouse ISG15 and Mx2 detected by quantitative RT-PCR.

B

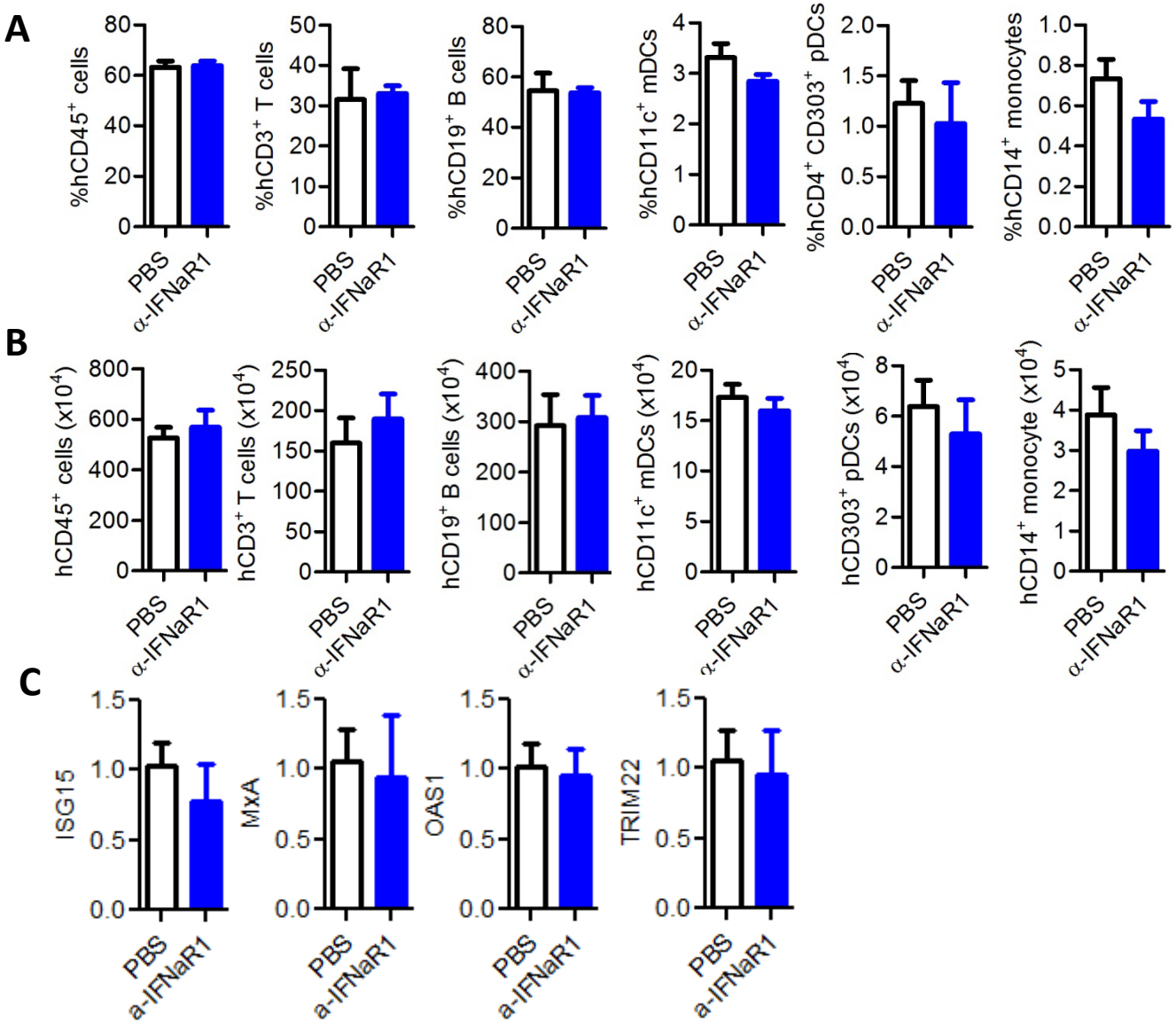




Supplemental Figure 3. Anti-IFNaR1 mAb efficiently block R848 induced ISGs *in vivo* in humanized mice.

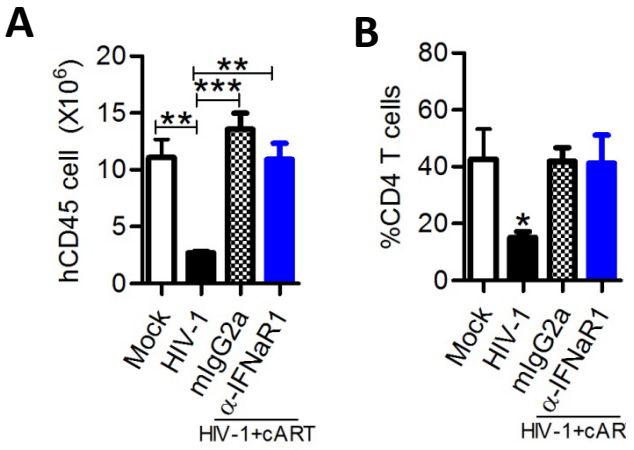
(A) Schematic diagram of the experimental design. Humanized mice were pretreated with PBS , Isotype control (mouse IgG2a) or α-IFNaR1 antibody (200ug/mouse, intraperitoneal injection), and 6 hours later, the mice received PBS or R848 (20ug/mouse, intraperitoneal injection) treatment. At 18 hours, peripheral blood cells were collected for analysis. **(B)** The relative mRNA levels of human Mx2, ISG15, OAS-1, and IRF7 were detected by real-time PCR. Shown are combined data of two independent experiments (PBS, n=10; R848+mIgG2a, n=9; R848+ α-IFNaR1, n=9) with mean values ± s.e.m. *P < 0.05, **P < 0.01, ***P < 0.001. One-way analysis of variance (ANOVA) and Bonferroni's post hoc test.

Supplementary Fig.4

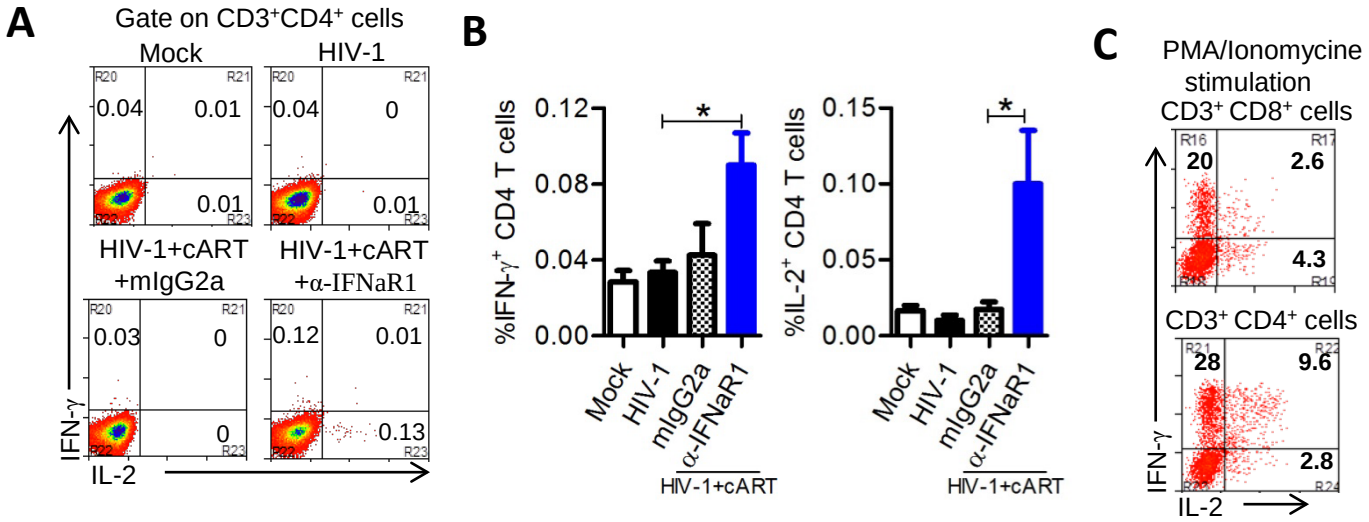


Supplemental Figure 4. Anti-IFNaR1 mAb treatment *in vivo* does not affect human immune cell percentage and number in humanized mice.

Humanized mice were treated with PBS or α-IFNaR1 mAb (200ug/mouse, i.p.). Mice were sacrificed 24 hours later. The percentages **(A)** and numbers **(B)** of human total immune cells (hCD45$^+$), T cells (hCD45$^+$ CD3$^+$) , B cells (hCD45$^+$ CD19$^+$), myeloid DCs (hCD45$^+$ CD3$^-$ CD19$^-$ C D14$^-$ CD11c$^+$), plasmacytoid DCs (hCD45$^+$ CD3$^-$ CD19$^-$ CD11c$^-$ CD14$^-$ CD303$^+$) and monocytes (hCD45$^+$ CD14$^+$) in the spleen were shown. **(C)** Relative mRNA levels of OAS1 and IRF-7 in splenocytes were detected by realtime PCR. Shown are data from one experiment (PBS, n=3; α-IFNaR1, n=3) with mean values ± s.e.m.



Supplemental Figure 5. **cART rescue human immune cell number.**
Humanized mice were treated as in Fig.4a. Mice were sacrificed at 12 wpi. **(A)** Summarized data show numbers of total human leukocytes in spleen. **(B)** Summarized data show percentage of human CD4 T cells in total human leukocytes in spleen. Shown are combined data from two independent experiments with mean values ± s.e.m. (mock, n=7; HIV-1, n=7; HIV-1 + cART + mIgG2a, n=8; HIV-1 + cART + α-IFNaR1, n=8). *P < 0.05, **P < 0.01, ***P < 0.001. One-way analysis of variance (ANOVA) and Bonferroni's post hoc test.



Supplemental Figure 6. **IFNaR blockade in cART-suppressed infection reverses HIV-specific T cell function.**

Humanized mice were treated as in Fig.4a. Splenocytes were stimulated *ex vivo* with HIV Gag peptide pools for 8 hours (BFA was added at 3 hours) followed by intracellular cytokine staining. **(A)**Representative dot plot show IFN-γ and IL-2 producing CD4 T cells. **(B)** Summarized data show percentages of IFN-γ and IL-2 producing CD4 T cells after Gag peptide pools stimulation. **(C)** Mix splenocytes from the mice were stimulated with PMA/Ionomycine as positive control. Representative dot plot show IFN-γ and IL-2 producing CD8 and CD4 T cells 4 hours after PMA/Ionomycine. Shown are combined data **(B)** from two independent experiments with mean values ± s.e.m. (mock, n=7; HIV-1, n=7; HIV-1 + cART + mIgG2a, n=8; HIV-1 + cART + α-IFNaR1, n=8). *P < 0.05, **P < 0.01, ***P < 0.001. One-way analysis of variance (ANOVA) and Bonferroni's post hoc test.