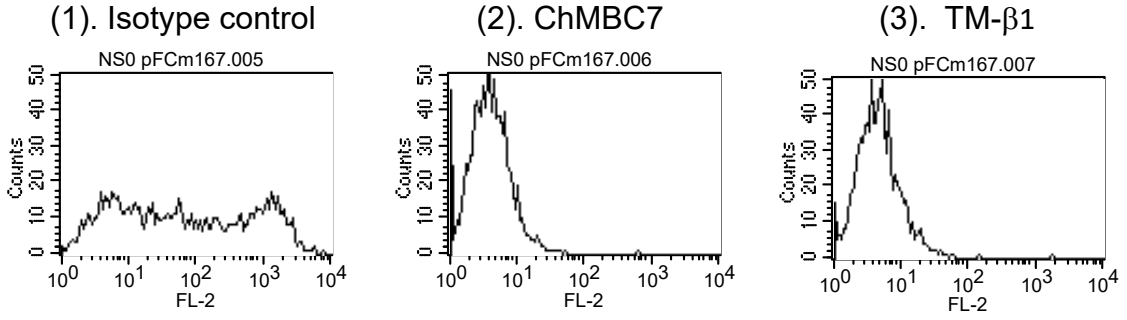
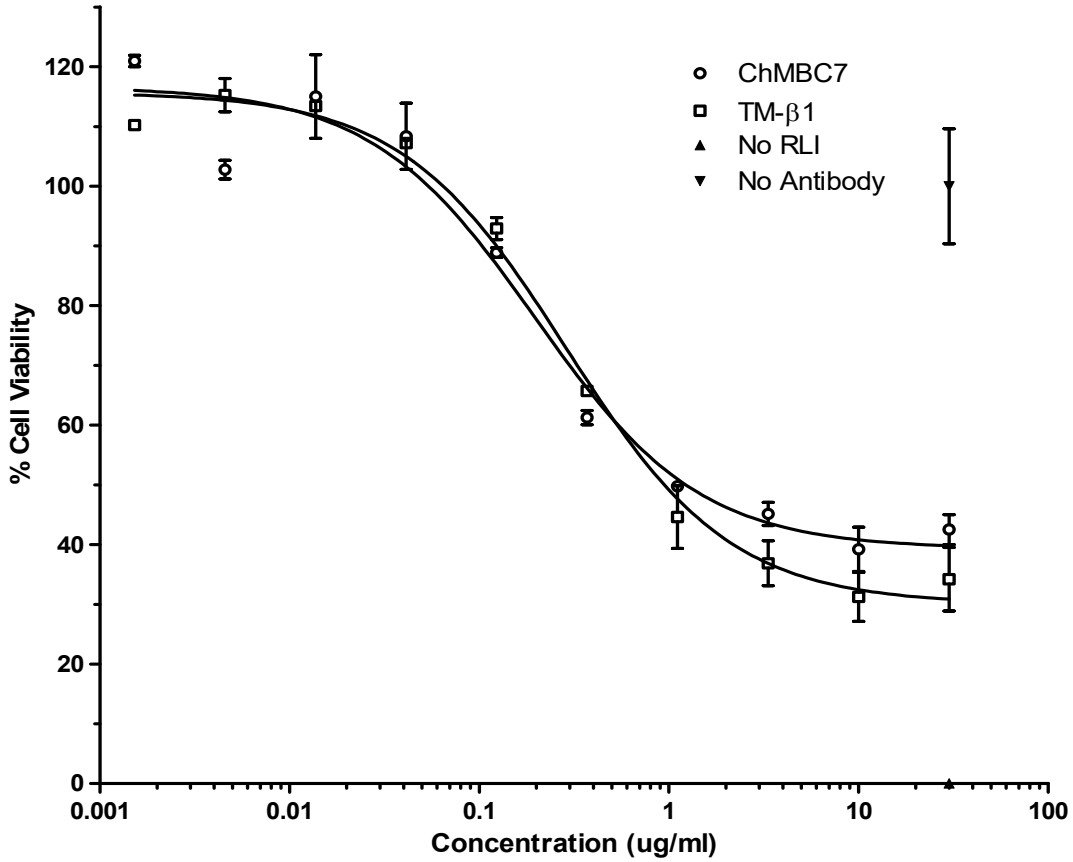
Supplemental Figure 1



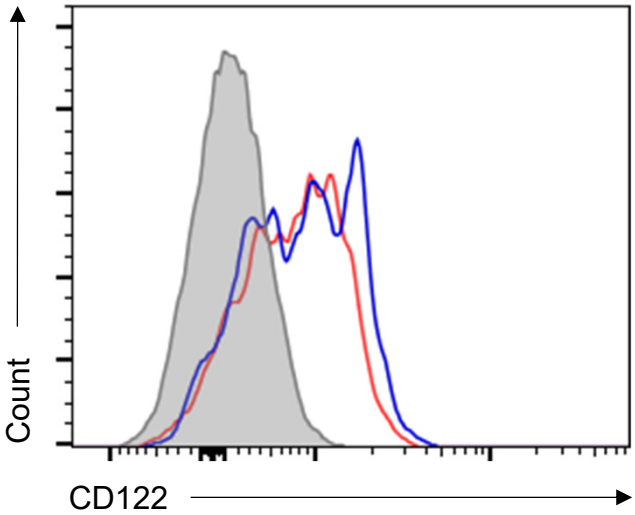
Supplemental Figure 1. ChMBC7 and TM-β1 bind to the same epitope of mouse CD122. NS0 transfectant cells expressing surface-bound CD122 were pre-incubated with 10 ug/ml of (1) IgG2a control antibody MOPC-173, (2) ChMBC7, or (3) TM-β1 for 30 min before probed with 0.4 ug/ml PE-conjugated TM-β1 (BioLegend Cat# 123210) for an additional 20 min. The cells were then washed and analyzed for CD122 detection by flow cytometry.

Supplemental Figure 2



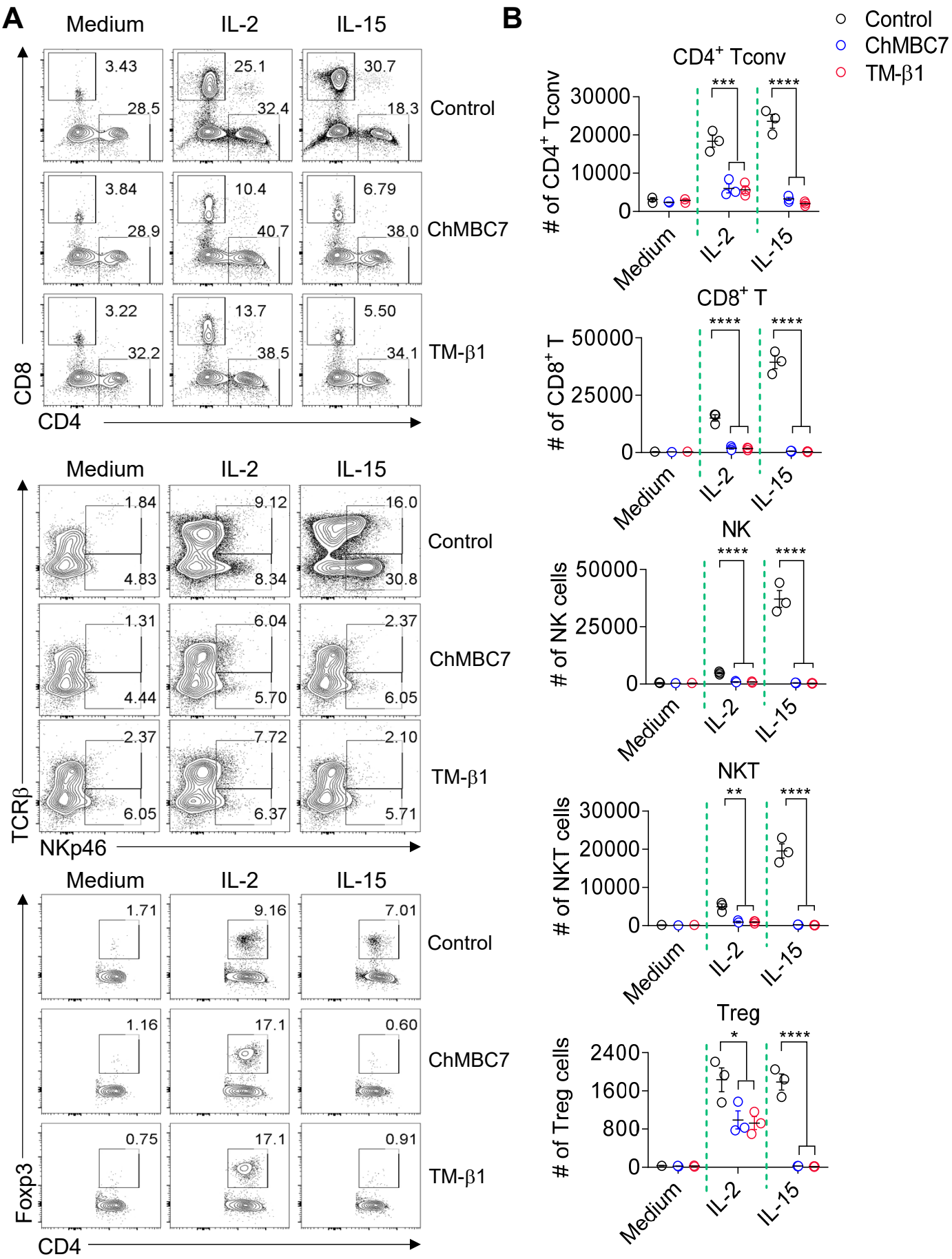
Supplemental Figure 2. ChMBC7 and TM-β1 have a similar potency in inhibiting IL-15 transpresentation. Serially-diluted ChMBC7 or TM-β1 was added to CTLL-2 cells grown in the presence of IL-15/human IL-15Rα sushi domain complex (RLI) at 50 ng/ml. Cell proliferation was determined after 3 days by the Celliter Glo Assay (Promega, Madison, WI).

Supplemental Figure 3



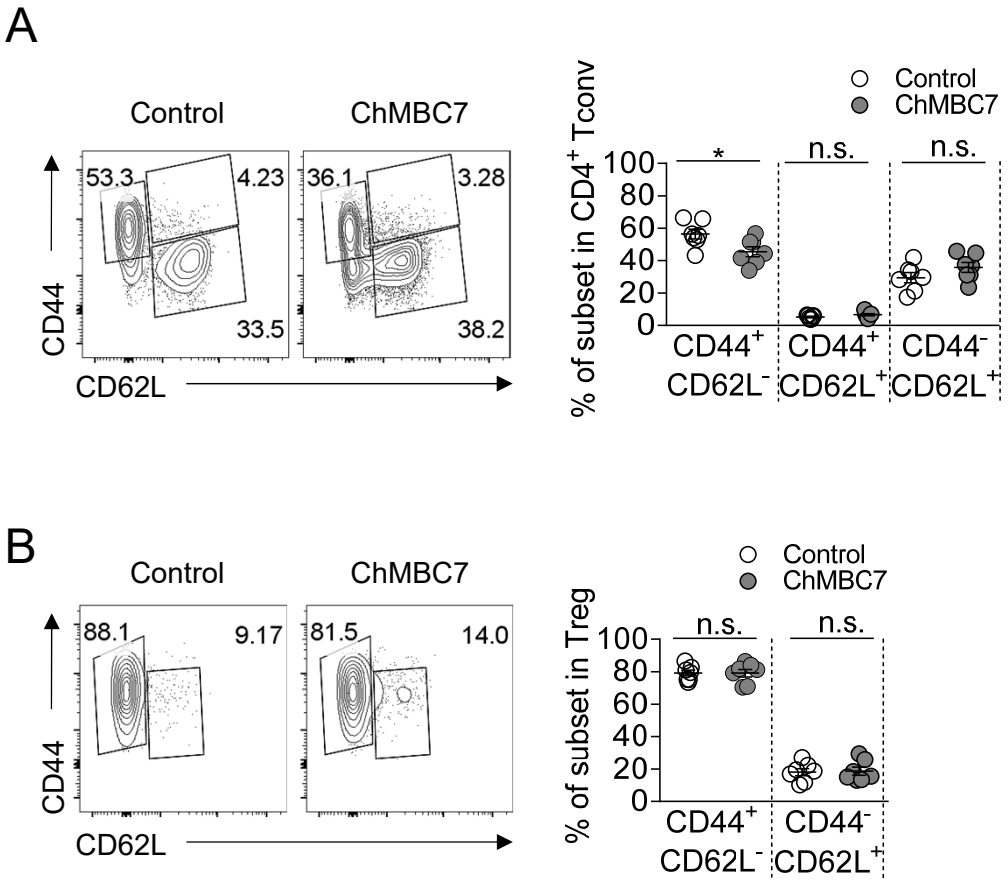
Supplemental Figure 3. Collagenase digestion does not affect the detection of CD122 expression. Half of the spleen from pre-diabetic NOD mouse was digested using the same procedure as we did for pancreas (see Method for details). The other half of the spleen was processed by mechanic disruption. The expression of CD122 in NKp46^{+} NK cells was measured by flow cytometry. Grey, isotype control; blue, non-digested spleen; red, digested spleen. Shown are representative FACS data from two experiments.

Supplemental Figure 4



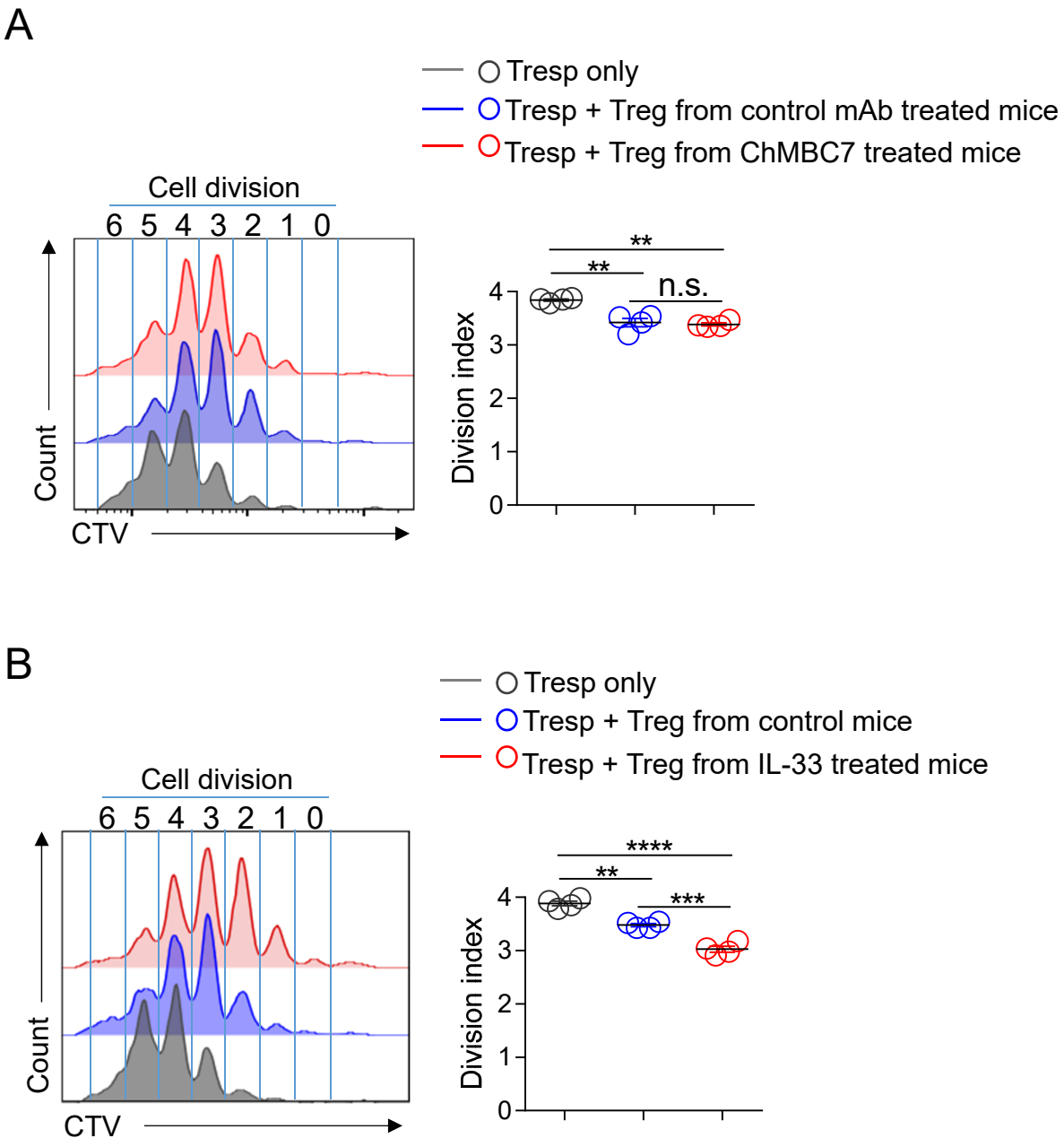
Supplemental Figure 4. CD122 blockade suppresses the proliferation and survival of CD8$^+$ T cells and NK cells in vitro. Total splenocytes were cultured for 7 days with IL-2 or IL-15, in the presence of control mAb, ChMBC7, or TM-β1, respectively. (**A**) Representative FACS plots of various immune cell populations. (**B**) Statistics of the numbers of each subset. Data are representative of three independent experiments. P values are calculated using one-way ANOVA with a Turkey multiple comparison test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$; n.s. non-significant.

Supplemental Figure 5



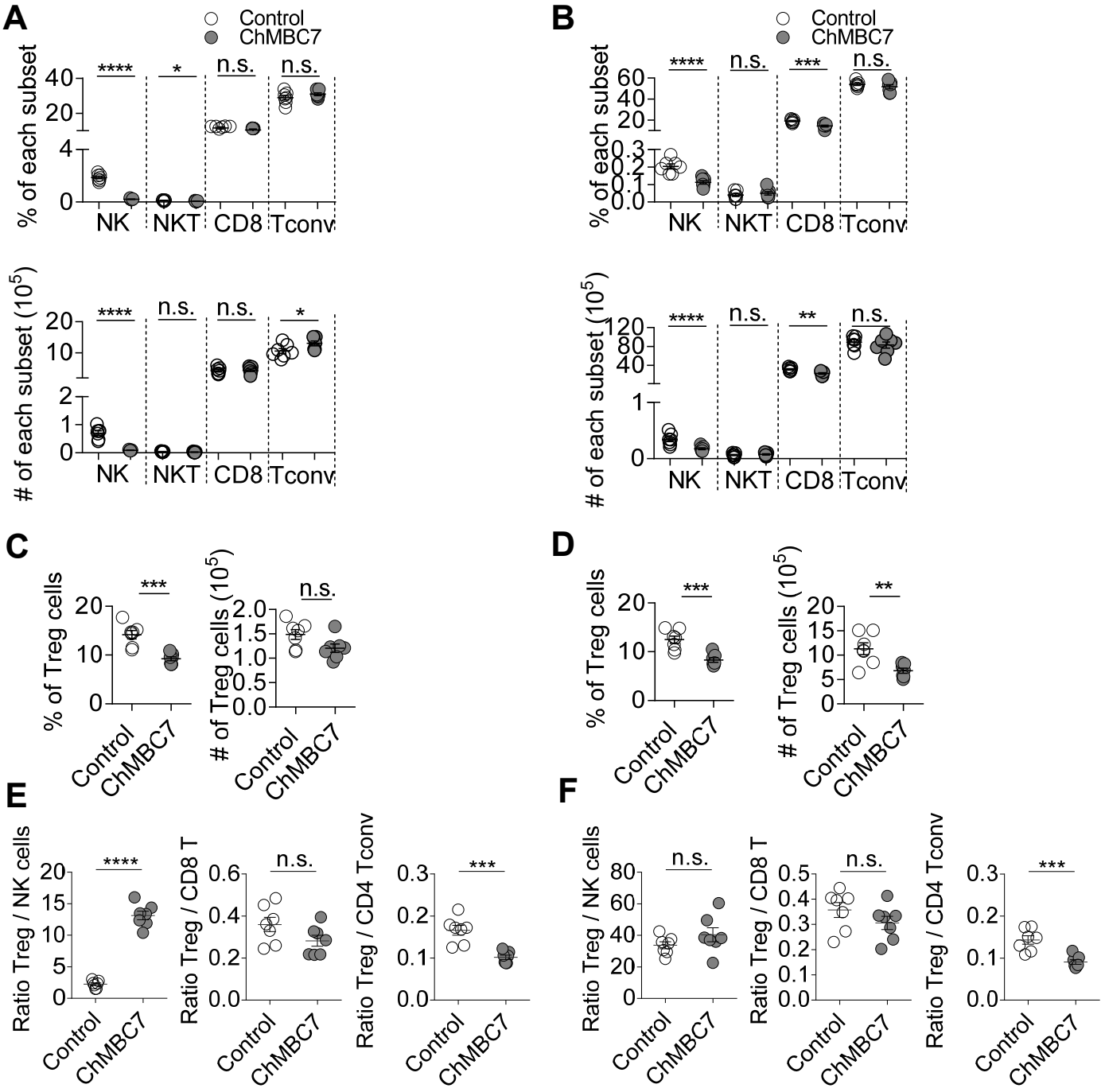
Supplemental Figure 5. CD122 blockade alters T cell activation. Representative FACS plots (left) and statistics (right) of CD4⁺ Tconv (**A**) and Treg (**B**) subsets from mice as in Figure 4 A-C (n=7). P values are calculated using Student's *t* test. * $p < 0.05$; n.s. non-significant.

Supplemental Figure 6



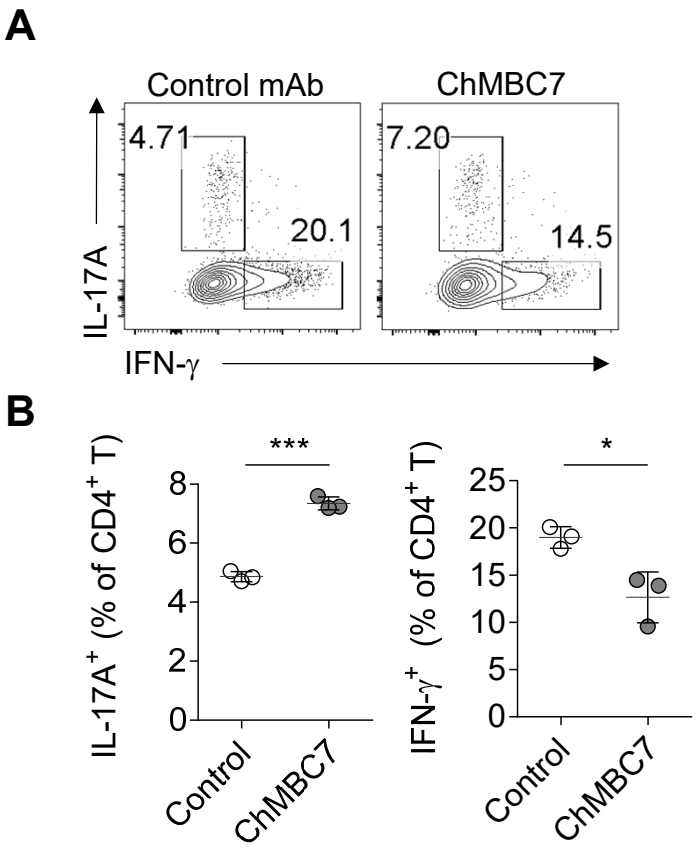
Supplemental Figure 6. In vitro suppression assay of Treg cells from mice treated with control mAb, ChMBC7 or IL-33. (**A**) Representative (left) and statistical analysis (right) of responder T cells (Tresp) proliferation cocultured with Treg cells from control mAb or ChMBC treated mice at 1:1 ratio. (**B**) Representative (left) and statistical analysis (right) of Tresp proliferation cocultured with Tregs from control or IL-33 treated mice at 1:1 ratio. Data are representative of one experiment (n=4). P values are calculated using Student's *t* test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$; n.s. non-significant.

Supplemental Figure 7



Supplemental Figure 7. The effect of CD122 blockade in peripheral lymphoid organs. Mice were the same as in Figure 4. The percentages and numbers of indicated cell types in spleen (**A**) and pancreatic lymph nodes (**B**). The percentages and numbers of Treg cells in spleen (**C**) and pancreatic lymph nodes (**D**). The ratios between Treg cells and pathogenic cells in spleen (**E**) and pancreatic lymph nodes (**F**). Statistical data are mean ± SEM. Data are representative of three independent experiments. P values are calculated using Student's *t* test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$; n.s. non-significant.

Supplemental Figure 8



Supplemental Figure 8. The effect of anti-CD122 on Th cell differentiation in vitro. Total splenocytes from NOD/BDC2.5 were cultured with BDC2.5 mimotope, in the presence of control mAb or ChMBC7 for 3 days. Shown are representative FACS plots (**A**) and (**B**) statistics of IL-17A$^+$ or IFN-γ$^+$ cells within CD4$^+$ Tconv cells after culture. Data are representative of three independent experiments. P values are calculated using Student's *t* test. * $p < 0.05$*** $p < 0.001$; n.s. non-significant.