Supplementary Figure Legends

Supplemental Figure 1. A. Survival curves of Foxp3mut, IL1R1$^{-/-}$Foxp3^{mut}, TLR2$^{-/-}$ Foxp3^{mut}, TLR4$^{-/-}$Foxp3^{mut} and TLR5$^{-/-}$Foxp3^{mut} mice. **B.** Skin and lung inflammation in TLR2$^{-/-}$ Foxp3^{mut}, TLR4$^{-/-}$Foxp3^{mut} and IL1R1$^{-/-}$Foxp3^{mut} mice (H & E, 200X magnification). **C**. Phenotypic characteristics of Foxp3 and TLR/IL-1R1 single and double mutant mice at 30 d of age, including weight, alopecia, skin hemorrhages and dryness. **D.** Expression of cytokine transcripts in the skin of Foxp3 and TLR/IL-1R1 single and double mutant mice, determined by real time PCR analysis. Each point represents results obtained from one individual mouse. Results in panel **A** reflect 4-21 mice/group, and in panels **B-D** of 4-10 mice/group, derived from 4-7 independent experiments. *p<0.05; **p<0.01, ***p<0.001.

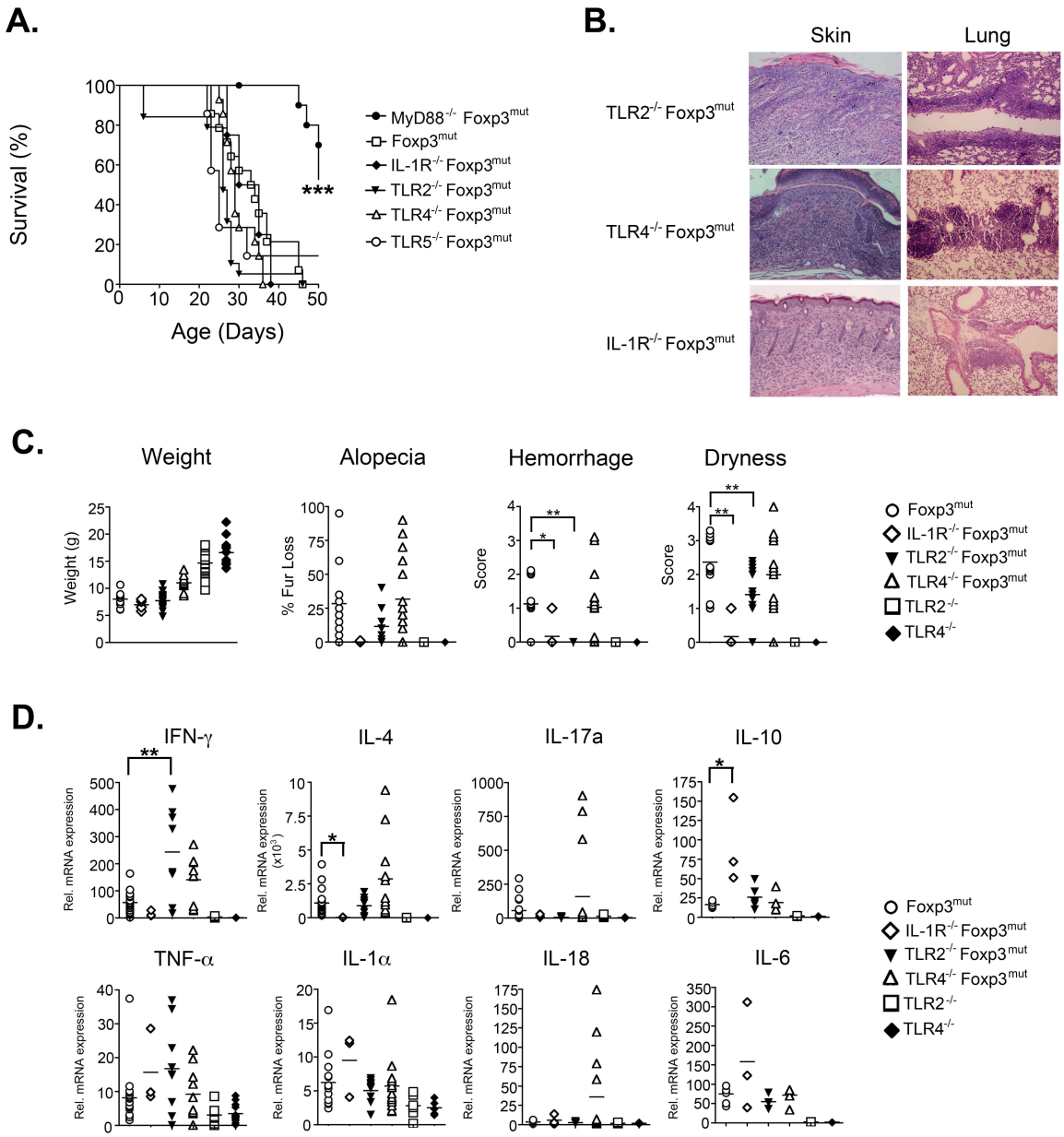
Supplemental Figure 2. Characteristics of the lymphoproliferative disease in the spleens of Foxp3^{mut} versus MyD88$^{-/-}$Foxp3^{mut} mice. **A.** Total lymphocyte counts and absolute cell numbers of CD4^{+} effector memory T cells (CD4^{+}CD62L^{low}CD44^{high}), CD8^{+} T cells and B220^{+} B cells in the draining lymph nodes of the respective genotype. **B**. Enumeration of IL-17-, IFNγ- and IL-4- producing CD4^{+} T cells in the spleens of WT and mutant mice. **C.** Representative flow cytometric panels of the results shown in **B.** Results are representative of 3-5 experiments involving 5-10 mice/group.

Supplemental Figure 3. Early onset of the exaggerated autoimmune lymphoproliferation in MyD88$^{-/-}$Foxp3^{mut} mice. Total lymphocyte counts and absolute numbers of CD4^{+} effector memory T cells (CD4^{+}CD62L^{low}CD44^{high}), CD8^{+} T cells and

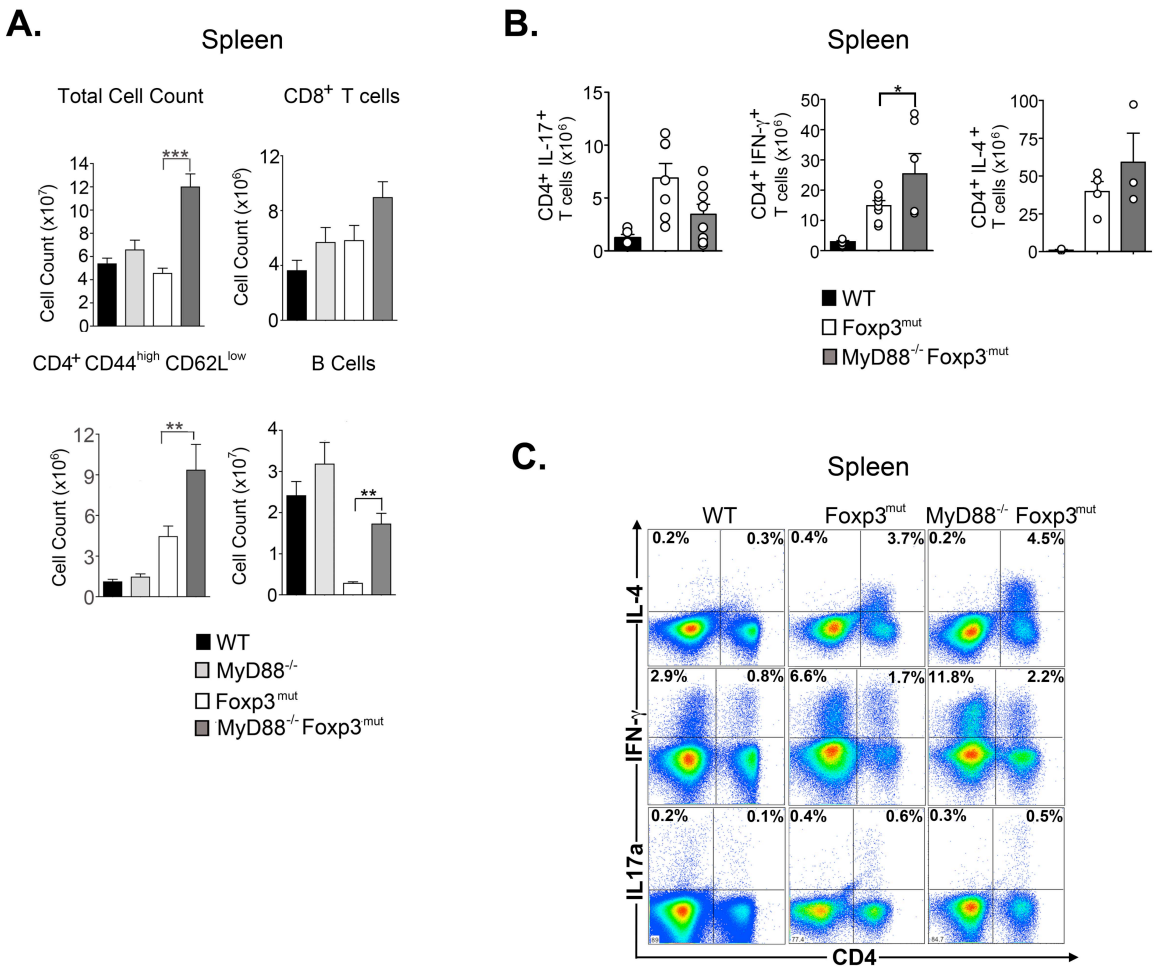
$B220^+$ B cells in the draining lymph nodes of WT, $MyD88^{-/-}$, $Foxp3^{mut}$ and $MyD88^{-/-}$ $Foxp3^{mut}$ mice were enumerated a 3 and 6 weeks of age. Results were obtained on 3-4 mice per group.

Supplemental Figure 4. Flow cytometric analysis of CD ligand (CD30L) and OX40 in T cells of WT, $Foxp3^{mut}$ and $MyD88^{-/-}Foxp3^{mut}$ mice. **A**. Flow cytometric profiles of OX40 and CD30L expression in $CD4^+$ naïve ($CD62L^{high}CD44^{low}$) and effector memory ($CD62L^{low}CD44^{high}$) T cells isolated form the draining lymph nodes and lings of the respective mouse strains. **B**. Percent expression of OX40 and CD30L in $CD4^+$ effector memory as compared to naïve T cells in the respective mouse strains. Results were obtained on 3-9 mice per group.

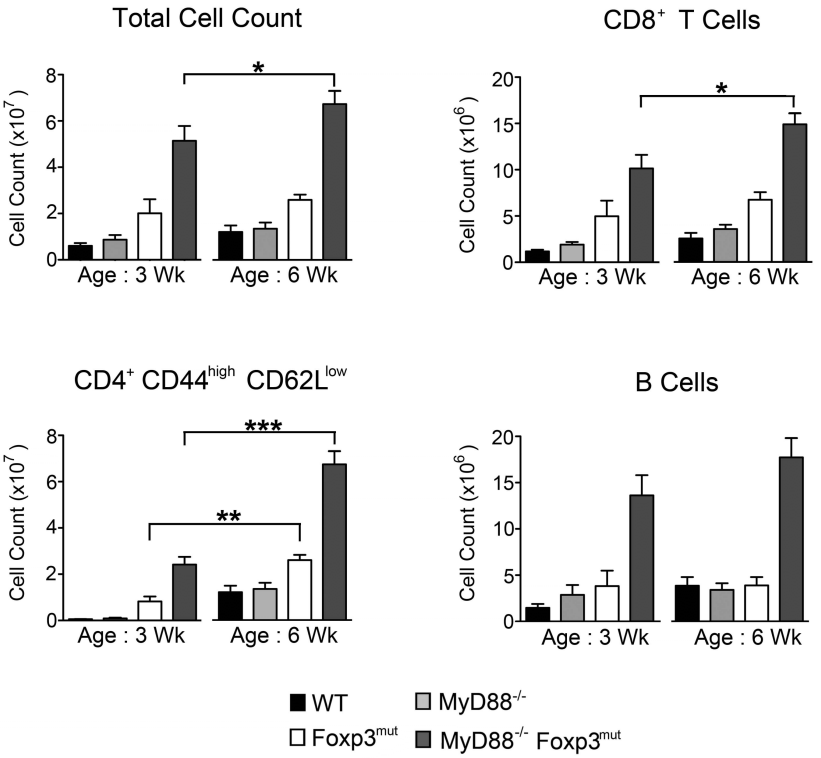
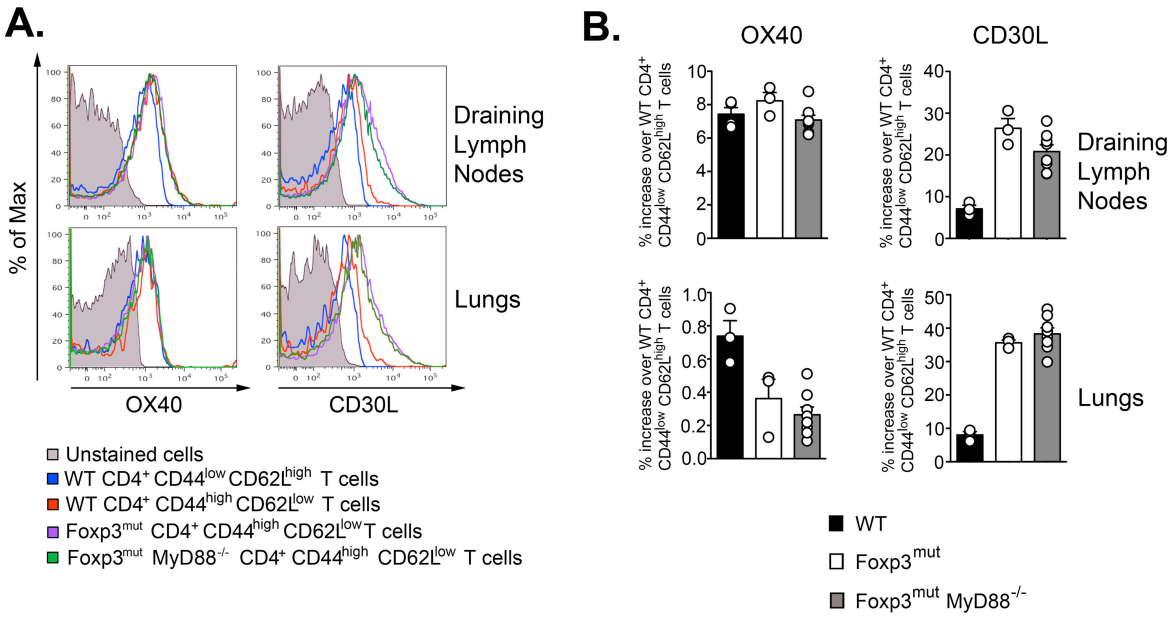
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4