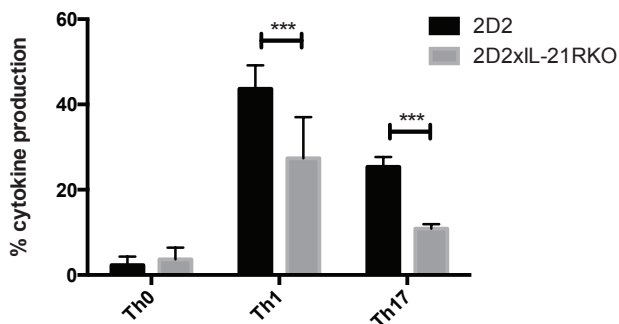
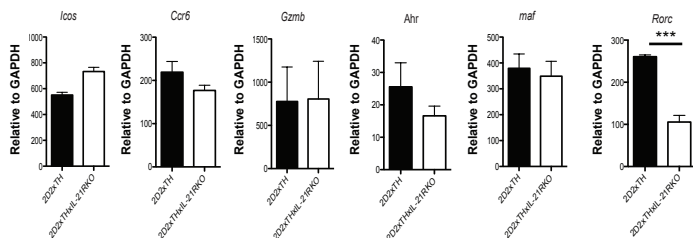




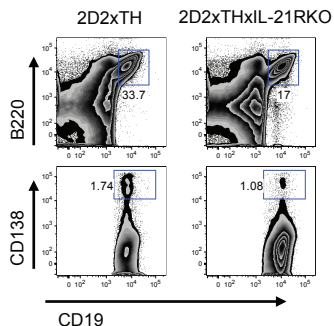
Supplementary Figure 1: The absence of IL-21R on CD4 T cells results in decreased IFN γ and IL-17

Quantification of signature cytokine from Th1 (IFN γ) or Th17 (IL-17) differentiated CD4 T cells. Naïve CD4 T cells were sorted from 2D2 or 2D2xIL-21R KO cells then differentiated with IL-12 (for Th1) or TGF- β 3+IL-6 (For Th17) cytokines for four days. Cells were harvested for intracellular cytokine analysis. Data is a representative of at least three independent experiments. ***p<0.001



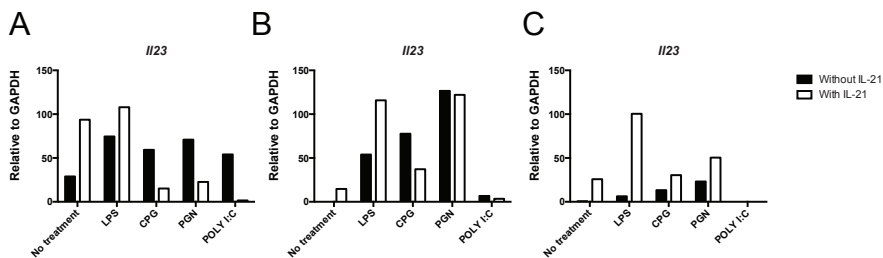
Supplementary Figure 2: Th17 pathogenic signature not regulated by the loss of IL-21R.

Quantitative RT-PCR of *Ccr6*, *Icos*, *Gzmb*, *Ahr*, *Maf*, *Rorc* mRNA in naïve 2D2xTH and 2D2xTHxIL-21R^{-/-} CD4⁺ T cells that were differentiated with TGF- β 3/IL-6 (Th17) for four days *in vitro*. Data is a representative of three independent experiments.



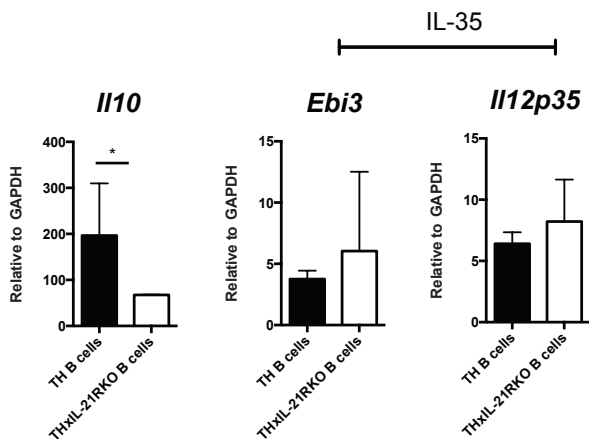
Supplementary Figure 3: Decreased frequency of TH B cells from 2D2xTHxIL-21RKO mice.

Steady state activation state of B cells stained with CD138⁺CD19⁺ and CD19⁺B220⁺ from the lymphoid tissues in healthy 2D2xTH and 2D2xTHxIL-21RKO mice. Data is a representative of two independent experiments.



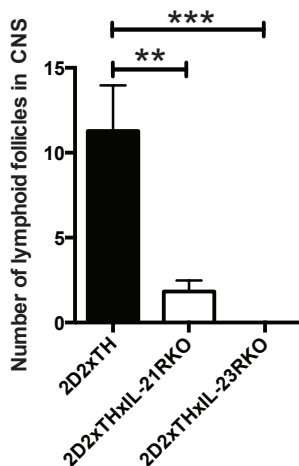
Supplementary Figure 4: IL-21 exposure promotes IL-23 in B cells under LPS stimulation

Wildtype B cells were activated *in vitro* with indicated stimulus and then harvested 24hr (A), 48hr (B), 72hr (C) post activation then quantified for *IL23* mRNA expression. B cells were sorted from C57BL/6 mice then cultured *in vitro*. Data is a representative of three independent experiments.



Supplementary Figure 5: THxIL-21RKO B cells produce less IL-10

Quantification of *Il10*, *Ebi3*, *Il12p35* mRNA expression in TH and THxIL-21RKO B cells that were sorted after 4 days of recall experiment with rMOG (10ug/ml). Data represents combined qPCR values from four independent experiments.



Supplementary Figure 6: Loss of IL-23R signaling completely abolished development of ectopic lymphoid follicles in 2D2xTH mice

Quantification of ectopic lymphoid follicles from the CNS of 2D2xTH and 2D2xTHxIL-21RKO mice that developed spontaneous EAE determined by a pathologist in a double blind manner. CNS from 2D2xTHxIL-23RKO mice were harvested at 3 months of age since no mice developed spontaneous EAE. Statistics were determined by Student's two tailed t test. ** $P < 0.01$; *** $P < 0.001$.