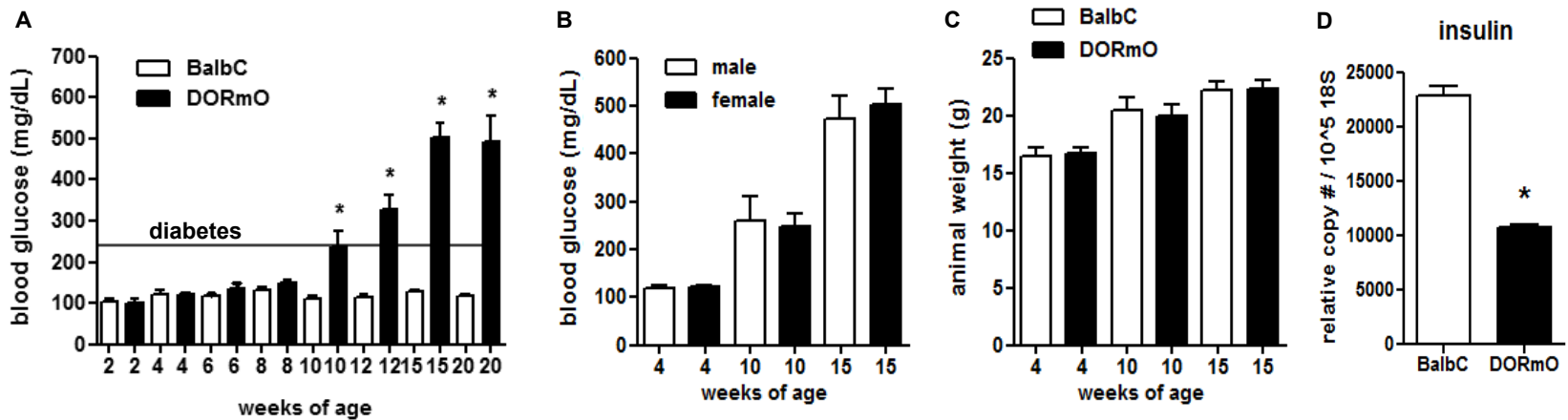
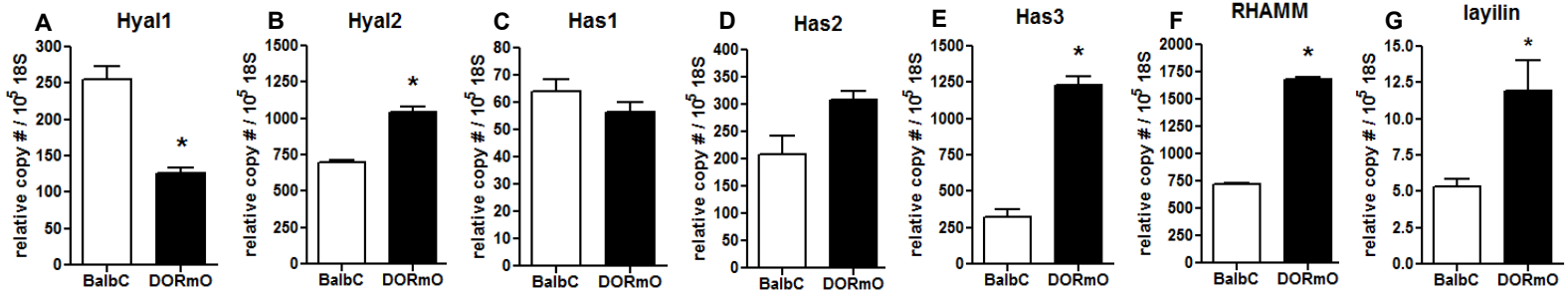


Supplemental Figure 1

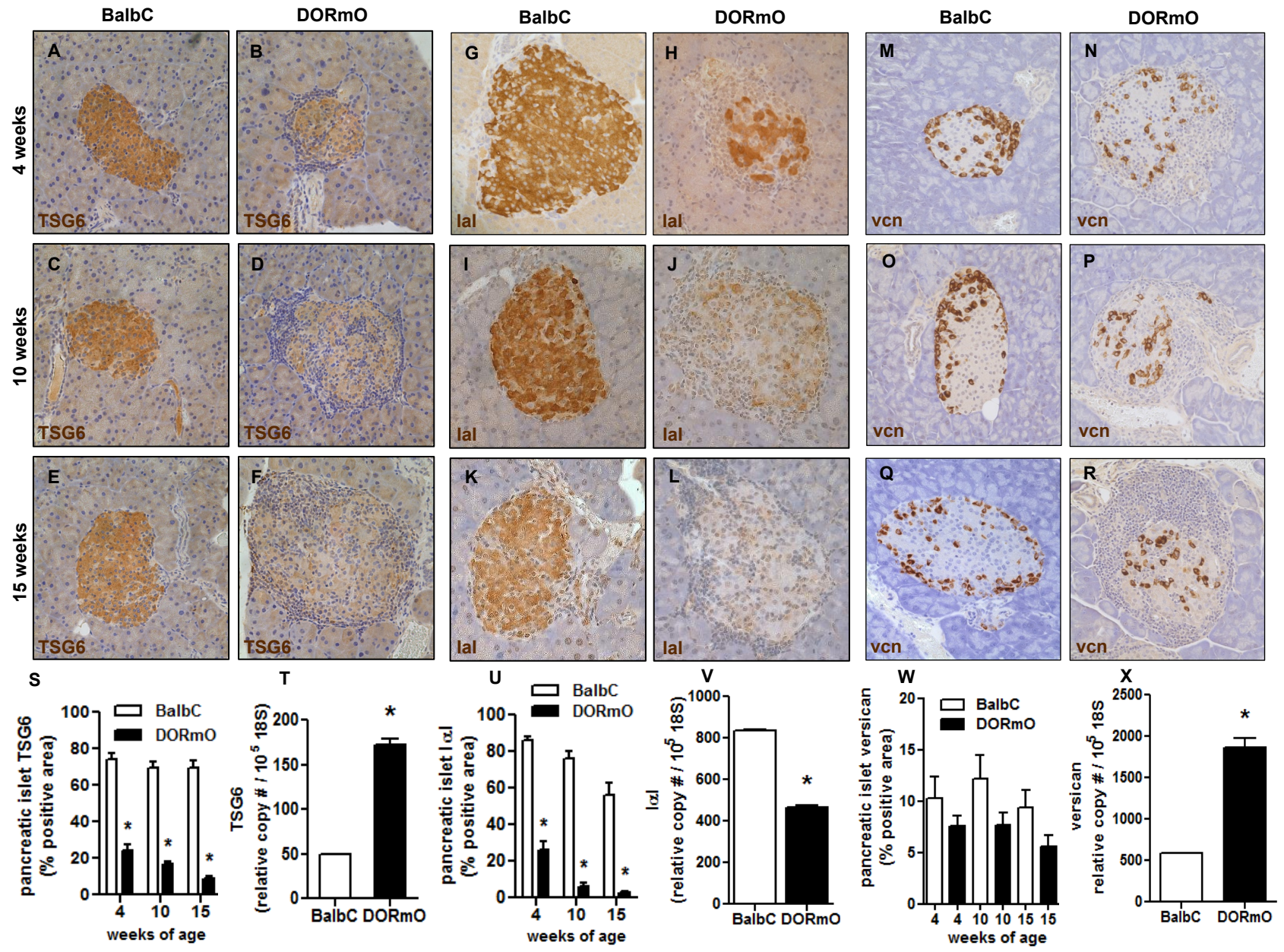


Supplemental Figure 1. Further characterization of diabetes in DORmO mice. **A.** Blood glucose of DORmO and BalbC (control) mice over time, n = 8-16. **B.** Blood glucose in male and female DORmO mice over time, n = 12-16. **C.** Mouse weight in BalbC (control) and DORmO mice over time, n = 12. **D.** Insulin mRNA expression for n = 200 islets collected from n = 6, 8-week-old BalbC and DORmO mice. Data represent mean ± SEM; *, p < 0.05 vs. control for each time point by unpaired t test.

Supplemental Figure 2

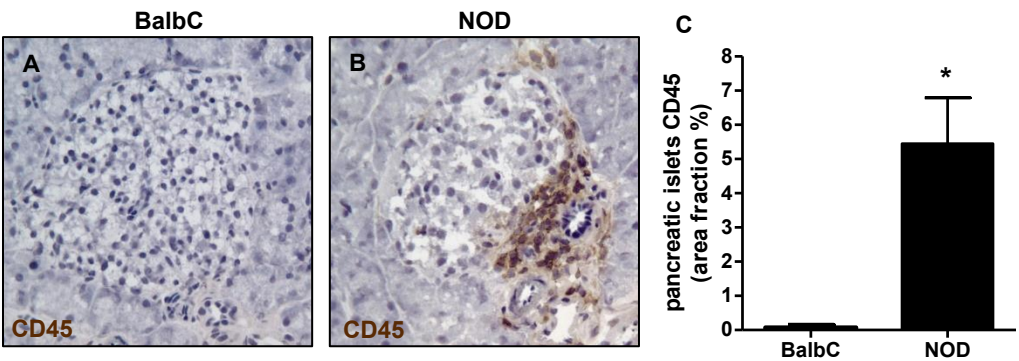


Supplemental Figure 2. HA-associated mRNA expression during diabetes progression. mRNA expression levels for two HA'ases (HYAL1 (A), HYAL2 (B)), three HA synthases (HAS1 (C), HAS2 (D), HAS3 (E)) and two HA receptors (RHAMM (F) and layilin (G)) all normalized to 18S expression levels. These data include isolated islets from 6 mice per condition taken at 8 weeks of age. Data represent mean ± SEM; *, p < 0.05 vs. control by unpaired t test.



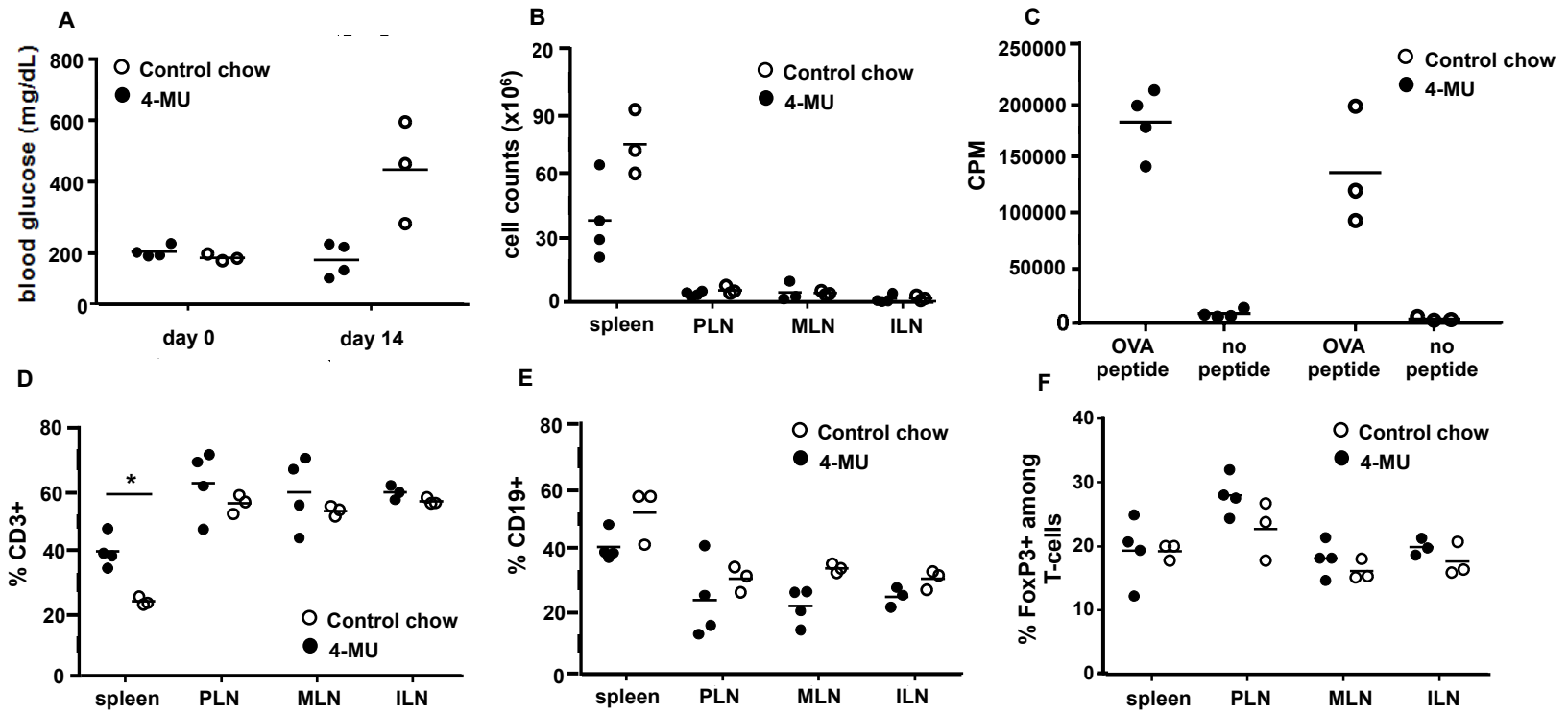
Supplemental Figure 3. TSG6, Ial, and versican levels during the progression of insulinitis. Representative histology for TSG6 (A-F), Ial (G-L) and versican (M-R) staining in DORmO and control mice over time. Percentage of islet area positive for TSG6 (S), Ial (U) and versican (vcn) (W) for DORmO mice and controls over time. mRNA expression of TSG6 (T), Ial (V) and versican (X) in BalbC and DORmO mice at 8 weeks of age. For S, U and W, at least 25 islets were visualized per mouse and data are for n = 6 mice per condition. For T, V, and X, data include information from at least 200 islets from n = 6 mice per time point. Magnification = 40x, data represent mean ± SEM; *, p < 0.05 vs. control for each time point by unpaired t test.

Supplemental Figure 4



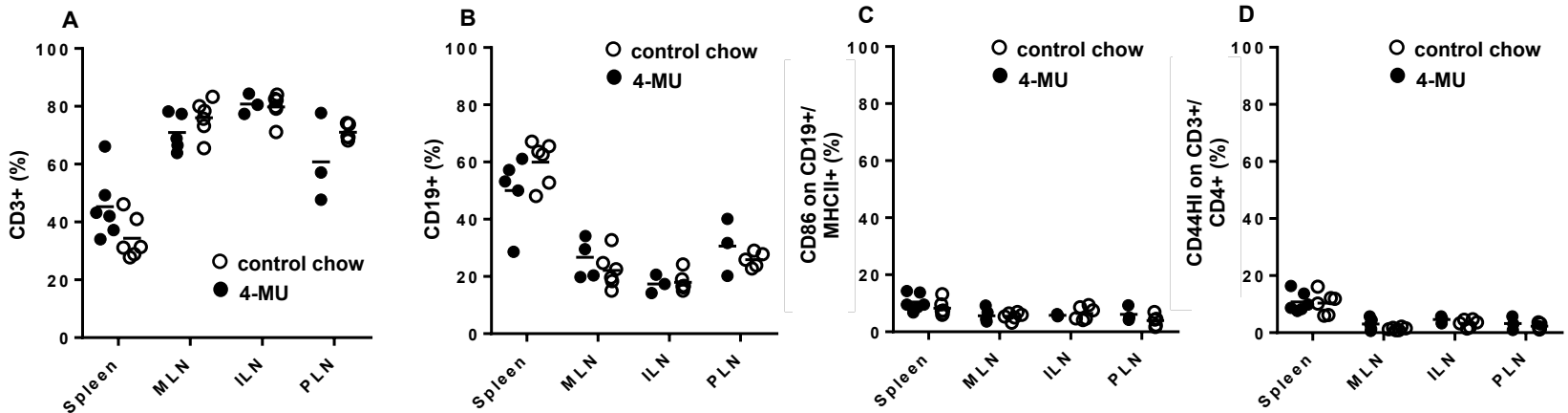
Supplemental Figure 4. NOD mice have leukocytic infiltrates in the pancreatic islets at an early age. Representative histologic staining of pancreas tissue from BalbC (control) (A) and NOD mice (B) stained for CD45 at 4-5 weeks of age. C. Average CD45 positive area of islets for these mice. At least 15 islets were visualized per mouse and data are for n = 3 mice per condition. Magnification = 40x, data represent mean ± SEM; *, p < 0.05 vs. control by unpaired t test.

Supplemental Figure 5



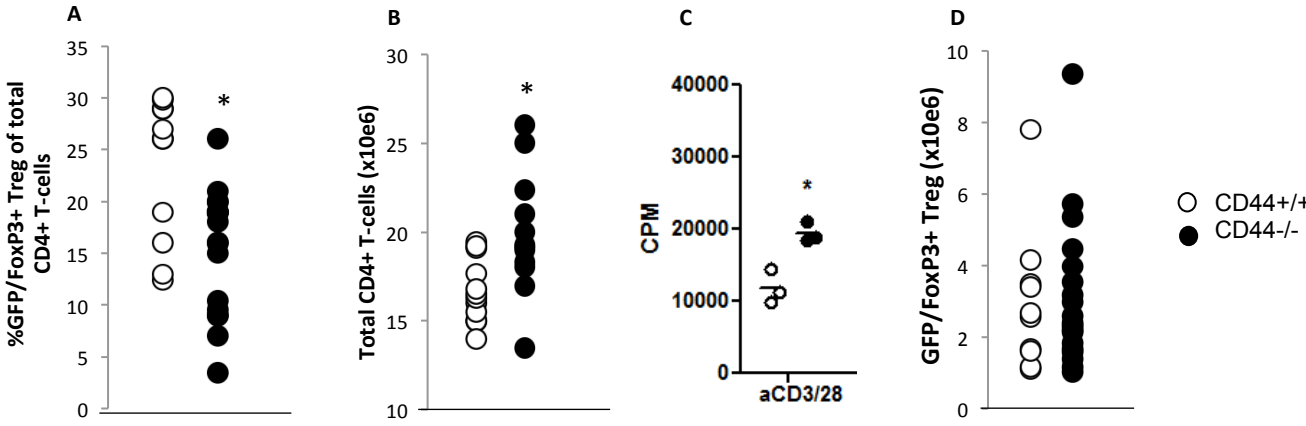
Supplemental Figure 5. Effects of 4-MU treatment on the immune profile of DORmO mice. DORmO mice were treated with 4-MU or control chow beginning at 8 weeks of age for 2 weeks. **A.** Blood glucose levels in these mice. **B.** Total cell counts in the spleen, MLN, ILN, and PLN. **C.** Proliferative responses of splenocytes to OVA at 10 or 1 µg/mL. **D-E.** The number of CD3+ T-cells (**D**) and CD19+ B-cells (**E**) present in the spleen, MLN, ILN, and PLN. **F.** The percentages of CD4+Foxp3+ Treg in the spleen, PLN, MLN, and ILN of these animals. N = 3-4 mice in each group. Data represent mean ± SEM; *, p < 0.05 vs. respective control by unpaired t test.

Supplemental Figure 6



Supplemental Figure 6. 4-MU effects on lymphocytes and activation markers. BalbC mice were started on 4-MU at 8 weeks of age and maintained on this therapy for two weeks. **A.** The percentage of CD3+ T-cells present in the spleen, MLN, ILN, and PLN in these same animals. **B.** The percentage of CD19+ B-cells present in the spleen, MLN, ILN, and PLN in these same animals. **C.** The percentages of CD86+CD19+MHC-II+ APC in these animals. **D.** The percentages of CD4+CD44+ activated effector T-cells in these animals. N = 3-6 mice in each group. Data represent mean ± SEM.

Supplemental Figure 7



Supplemental Figure 7. CD44^{-/-} mice have lymphocytosis and hyper proliferative T-cells. **A.** The percentage of CD4+GFP/Foxp3 Treg in spleens from CD44^{-/-} and CD44^{+/+} mice. **B.** Total CD4+ T-cell number in splenocytes from CD44^{-/-} and CD44^{+/+} mice. **C.** Proliferation measured as counts per minute (CPM) of CD4+ T-cells isolated from either CD44^{-/-} and CD44^{+/+} mice and activated with aCD3/28 Ab in vitro. **D.** Absolute number of CD4+GFP/Foxp3 Treg in spleens from CD44^{-/-} and CD44^{+/+} mice. For panels **A**, **B**, and **D**, n = 18 CD44^{-/-} mice and n = 10 CD44^{+/+} mice were used. Data represent mean ± SEM; *, p < 0.05 vs. respective control by unpaired t test.