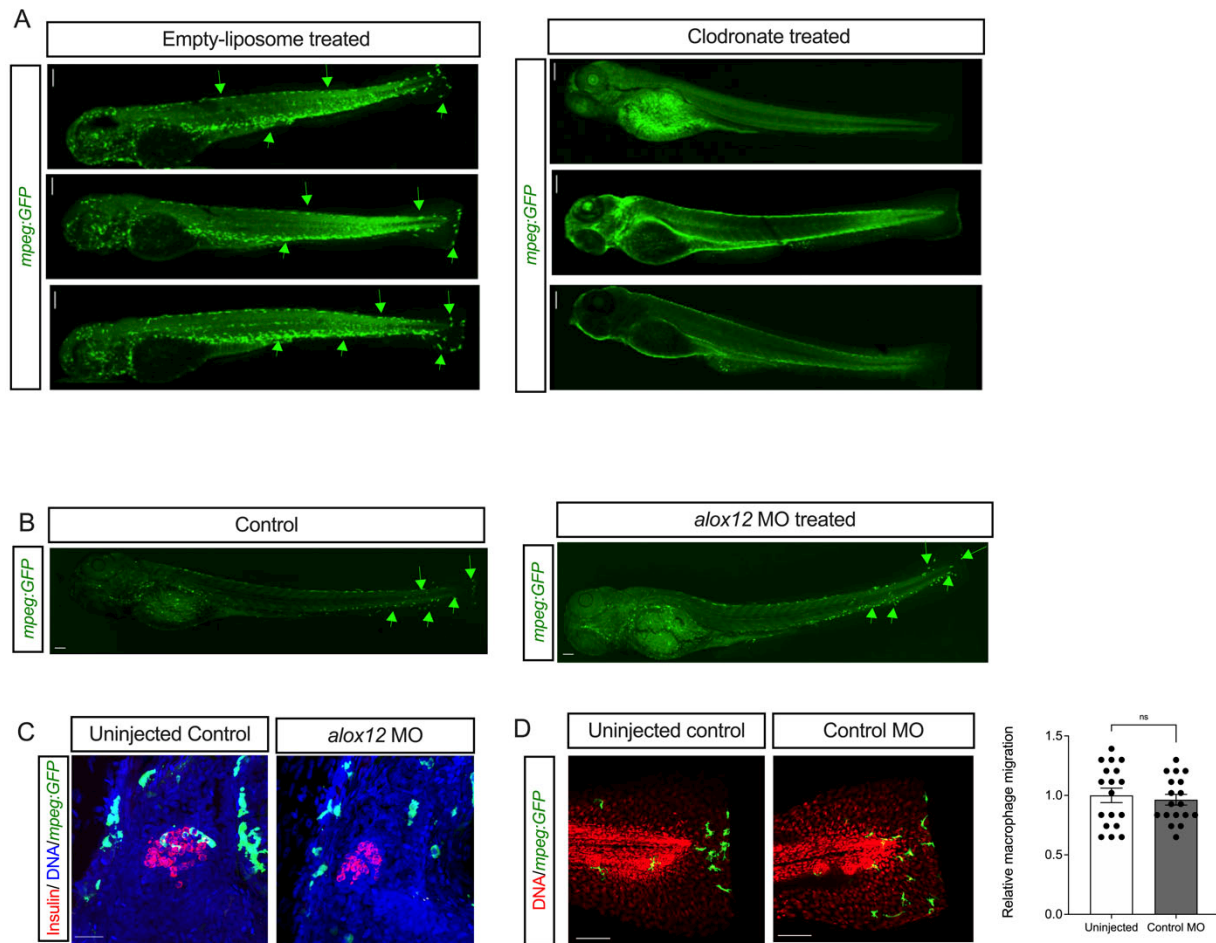
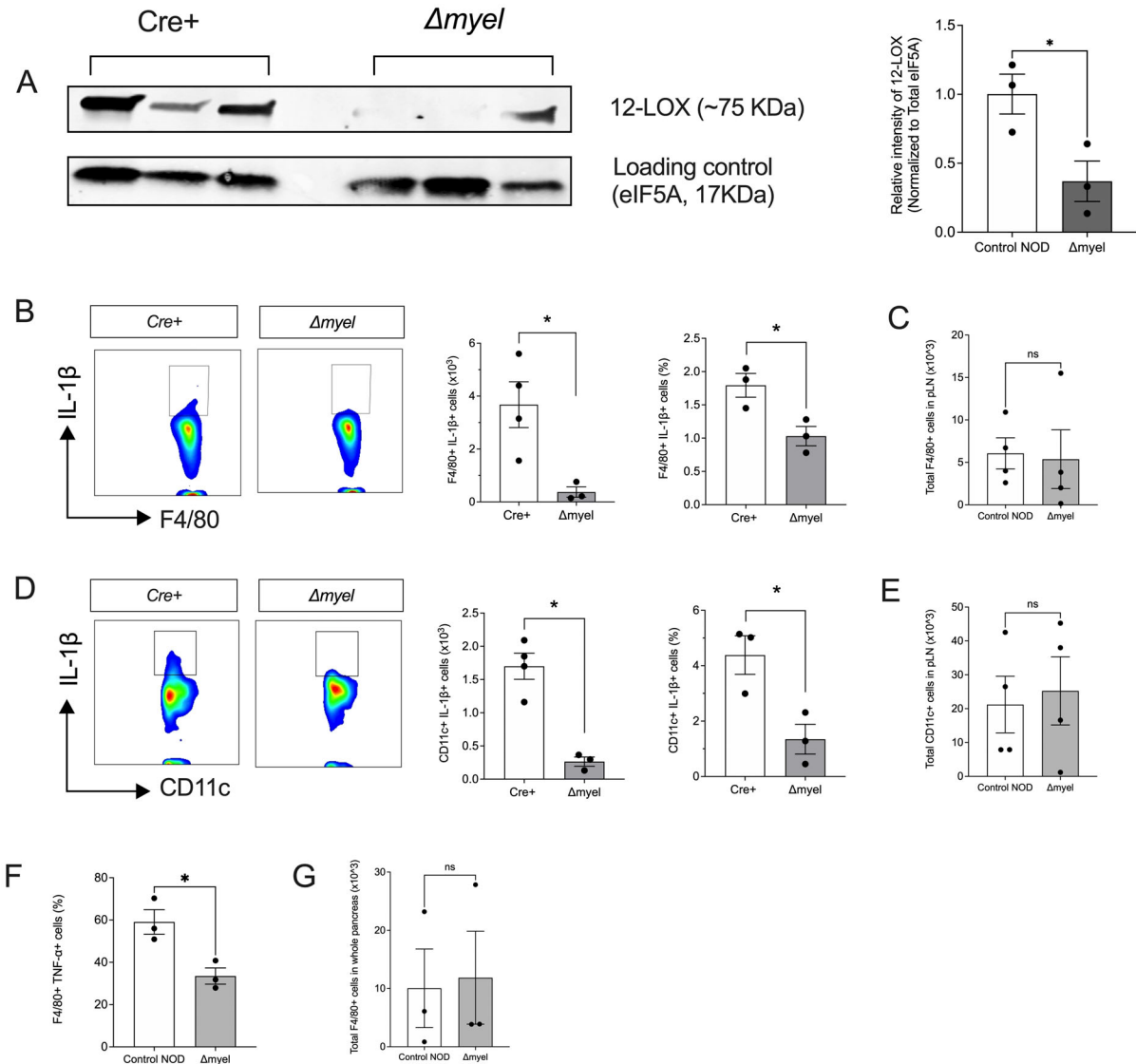
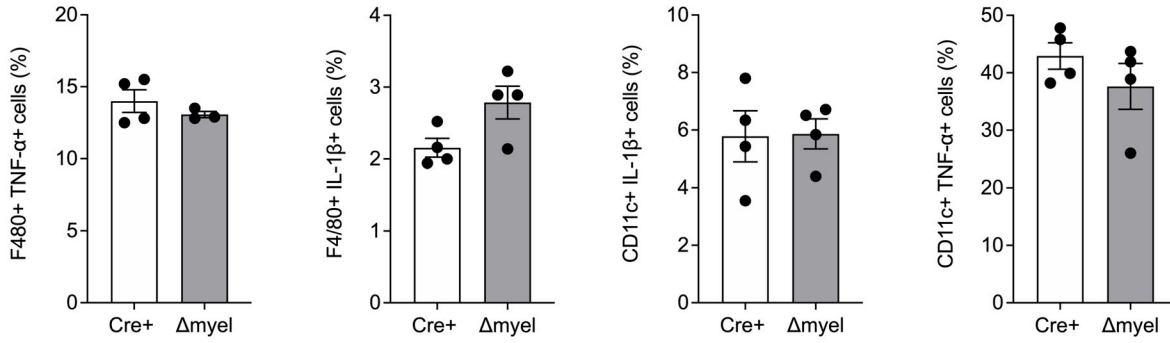




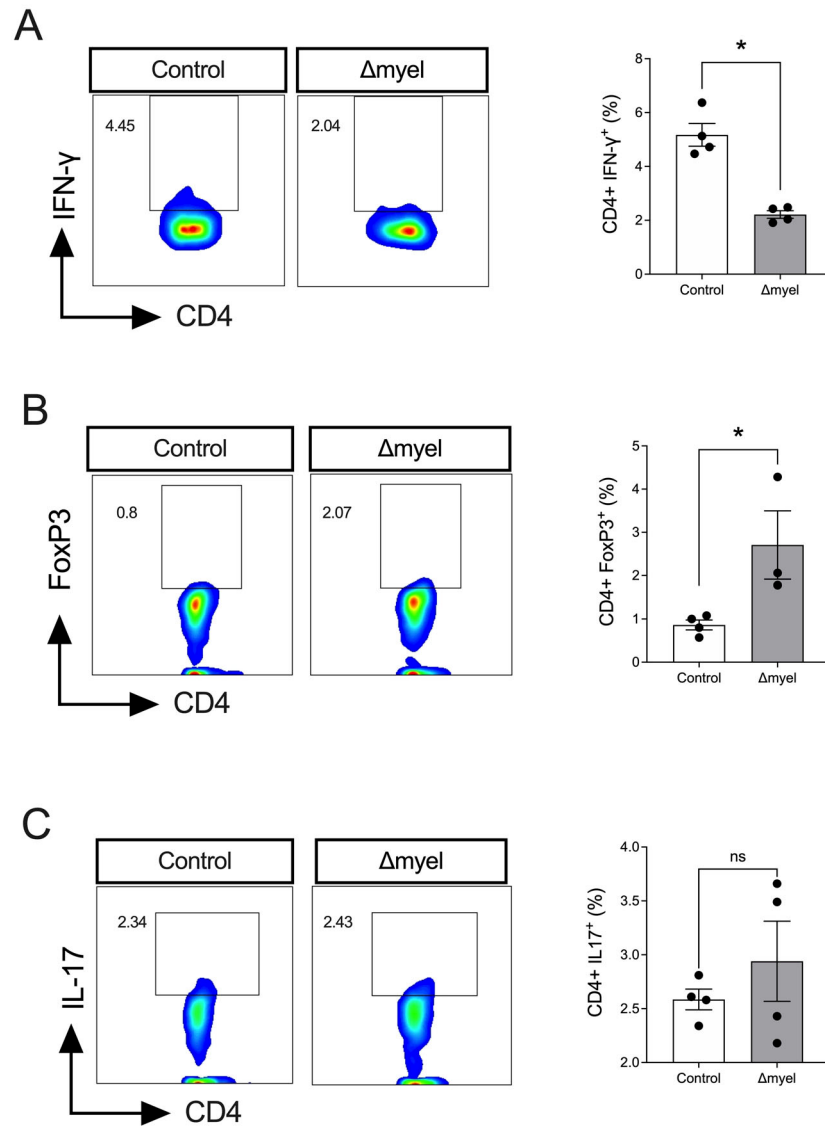
Supplementary Figure S1: Effect of clodronate liposomes and *alox12* MO on whole-embryo macrophages. (A) Three representative images of *Tg(mpeg:GFP)* zebrafish injected with empty control liposomes or with clodronate liposomes and stained for GFP (macrophages, green). Arrows indicate GFP+ macrophages; (B) Representative images of *Tg(mpeg:GFP)* zebrafish in control (uninjected) condition or injected with *alox12* MO. Arrows indicate GFP+ macrophages; (C) Representative images of islets from *Tg(mpeg:GFP);Tg(ins:NTR)* zebrafish treated with MTZ, then stained for insulin (β cells, red), GFP (macrophages, green), and DAPI (nuclei, blue). (D) Representative images of uninjected controls and control MO-injected *Tg(mpeg:GFP)* zebrafish tails after 6 hours of tailfin injury on left and quantitation on the right. * $P < 0.05$ by unpaired two-tailed t-test. Scale bars indicate 100 μ m.



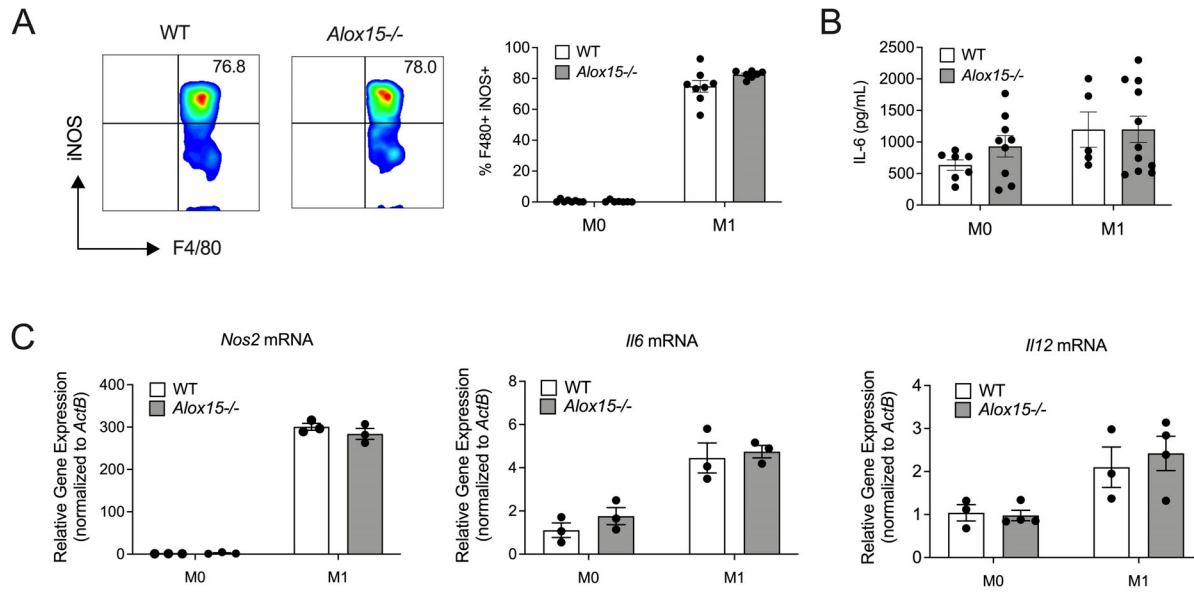
Supplementary Figure S2: Reduced proinflammatory myeloid cell populations in pancreatic lymph nodes of *NOD:Alox15 $\Delta myel$* mice. (A) Peritoneal cells were isolated from *NOD:Lyz2-Cre* (*Cre+*) control mice and *NOD:Alox15 $\Delta myel$* ($\Delta myel$) mice at 10 weeks of age and subjected to immunoblot analysis (left) and quantitation of the relative band intensities of 12-LOX normalized to the band intensities of eIF5A (right). $*P < 0.05$ by unpaired two-tailed t-test; (B) Pancreatic lymph nodes were isolated from *NOD:Lyz2-Cre* (*Cre+*) control mice and *NOD:Alox15 $\Delta myel$* ($\Delta myel$) mice at 8 weeks of age and subjected to flow cytometry analysis. Representative contour plot showing gating of F4/80+ IL-1 β + cells (left), total number of F4/80+ IL-1 β + cells (middle), and F4/80+ IL-1 β + cells as a percentage of total cells (right). $*P < 0.05$ by unpaired two-tailed t-test; (C) Quantitation of total number of macrophages (F4/80+ cells) in the pancreatic lymph nodes of *Cre+* and $\Delta myel$ mice. $*P < 0.05$ by unpaired two-tailed t-test; (D) Representative contour plot showing gating of CD11c+ IL-1 β + cells (left), total number of CD11c+ IL-1 β + cells (middle) and CD11c+ IL-1 β + cells as a percentage of total cells (right). $*P < 0.05$ by unpaired two-tailed t-test; (E) Quantitation of total number of dendritic cells (CD11c+ cells) in the pancreatic lymph nodes of *Cre+* and $\Delta myel$ mice. $*P < 0.05$ by unpaired two-tailed t-test; (F) Quantitation of total number of macrophages (F4/80+ cells). $*P < 0.05$ by unpaired two-tailed t-test; (G) proinflammatory macrophages (F4/80+ TNF- α + cells) in the whole pancreas of *Cre+* and $\Delta myel$ mice. $*P < 0.05$ by unpaired two-tailed t-test. All data are presented as mean $\pm$ SEM.



Supplemental Figure S3: Unaltered myeloid cell populations in spleen of control *NOD-Lyz2-Cre* and *NOD:Alox15^{Δmyel}* mice. Spleens were isolated from control *NOD-Lyz2-Cre* (*Cre+*) and *NOD:Alox15^{Δmyel}* (*Δmyel*) mice at 8 weeks of age and subjected to flow cytometry analysis for proinflammatory myeloid cell populations. Shown are the F4/80+ IL-1β+ cells, F4/80+ TNFα+ cells, CD11c+ IL-1β+ cells, and CD11c+ TNFα+ cells as a percentage of total cells. Data are presented as mean ± SEM.

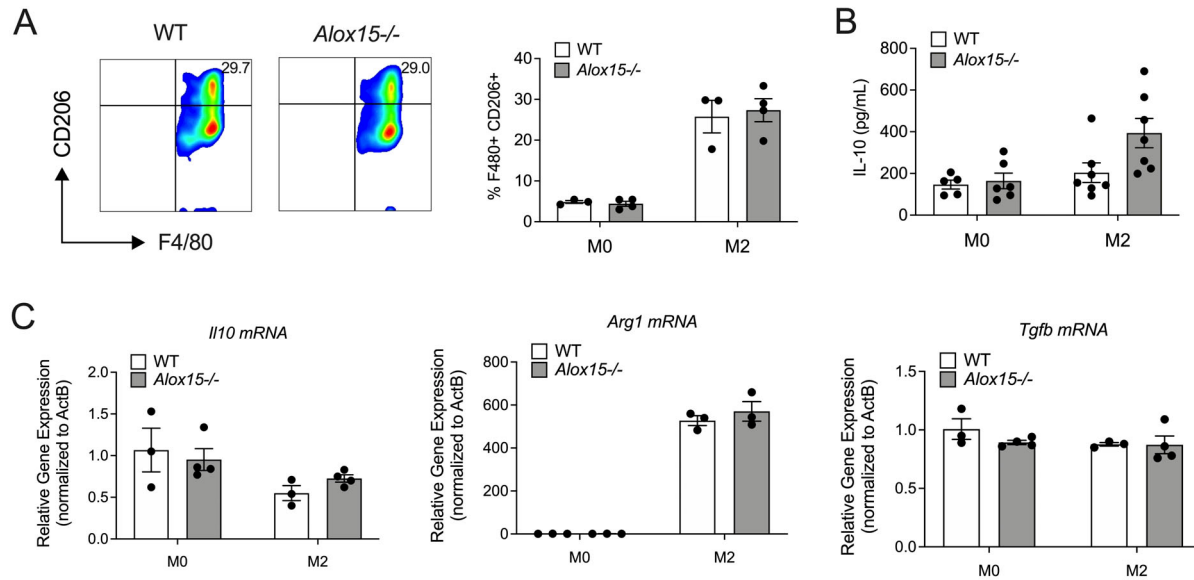


Supplemental Figure S4: Alterations in the T cell population of control *NOD-Lyz2-Cre* and *NOD:Alox15^{Δmyel}* mice. Pancreatic lymph nodes were isolated from control *NOD-Lyz2-Cre* (*Cre*⁺) and *NOD:Alox15^{Δmyel}* (Δ myel) mice at 8 weeks of age and subjected to flow cytometry analysis for T cell populations. Shown are the contour plots of (A) CD4+IFN- γ ⁺ cells, (B) CD4+Foxp3⁺ cells, and (C) CD4+IL-17⁺ cells on the left and the quantitation as a percentage of total cells on the right. **P*<0.05 by unpaired two-tailed t-test. Data are presented as mean $\pm$ SEM.



Supplemental Figure S5: Effect of 12-LOX depletion on “M1” polarization of macrophages.

Peritoneal cells were isolated from wildtype and *Alox15^{-/-}* mice and unpolarized (M0) or polarized in vitro to a “M1-like” state upon incubation with lipopolysaccharide (LPS) and IFN- γ , then subjected to flow cytometry analysis and quantitative RT-PCR. **(A)** Representative contour plot showing gating of F4/80+ iNOS+ cells is shown on the *left* and quantitation of F4/80+ iNOS+ cells as a percentage of total cells is shown on the *right*; **(B)** IL6 levels in media of unpolarized (M0) and M1-polarized cells; **(C)** quantitative RT-PCR data for the indicated genes (normalized to *Actb*). All data are presented as mean $\pm$ SEM. Statistics were evaluated by unpaired two-tailed t-tests for comparison between WT and *Alox15^{-/-}*.



Supplemental Figure S6: Effect of 12-LOX depletion on “M2” polarization of macrophages.

Peritoneal cells were isolated from wildtype and *Alox15^{-/-}* mice and unpolarized (M0) or polarized in vitro to a “M2-like” state upon incubation with IL-4, then subjected to flow cytometry analysis and quantitative RT-PCR. **(A)** Representative contour plot showing gating of F4/80+ CD206+ cells is shown on the *left* and quantitation of F4/80+ CD206+ cells as a percentage of total cells is shown on the *right*; **(B)** IL-10 levels in media of unpolarized (M0) and M2-polarized cells; **(C)** quantitative RT-PCR data for the indicated genes (normalized to *Actb*). All data are presented as mean $\pm$ SEM. Statistics were evaluated by unpaired two-tailed t-tests for comparison between WT and *Alox15^{-/-}*.