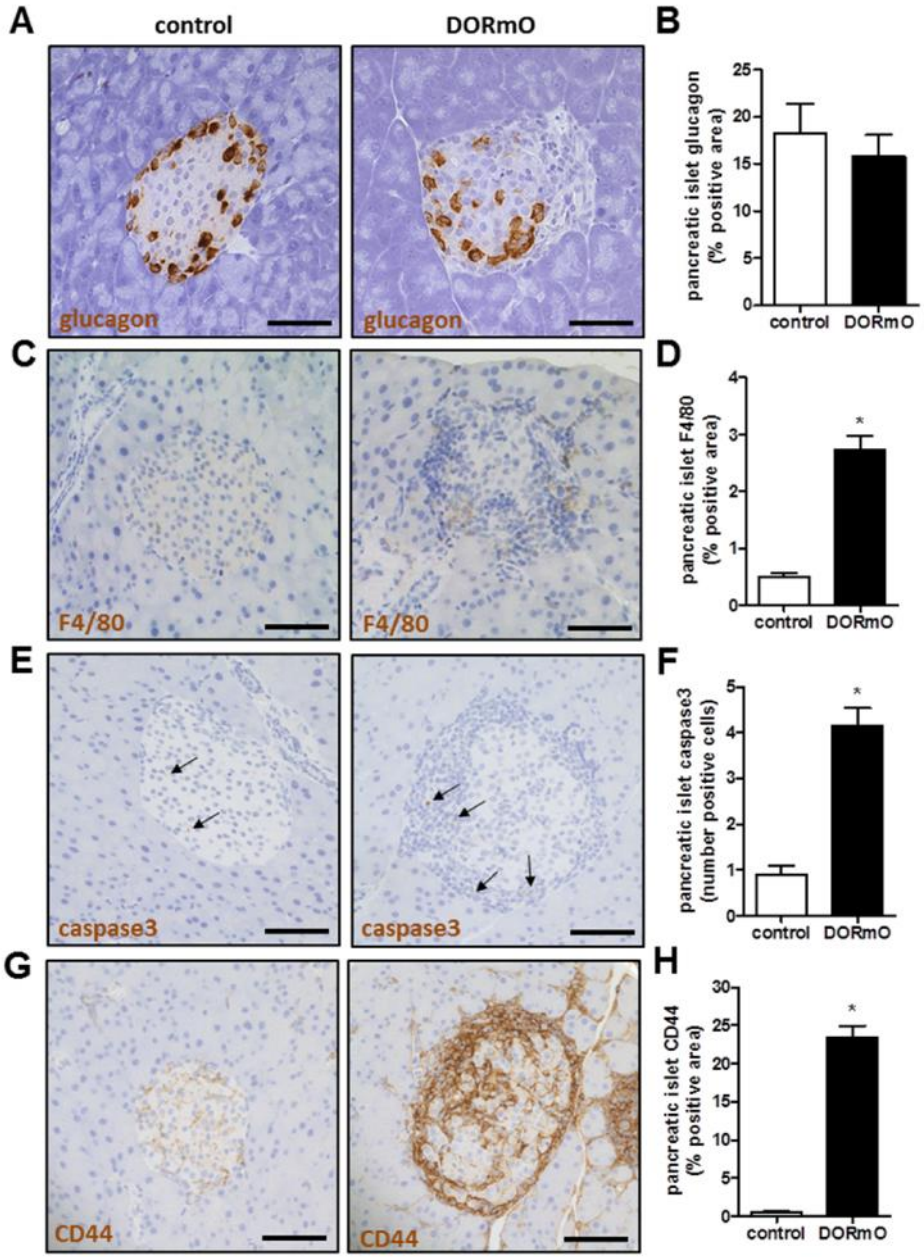
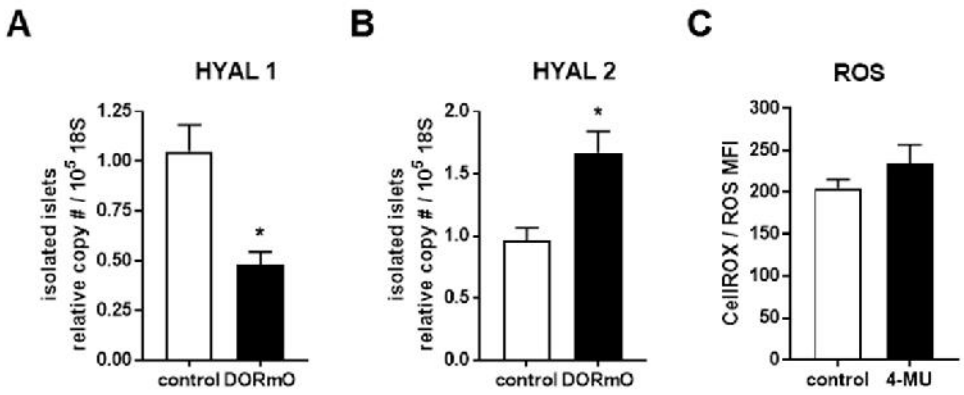
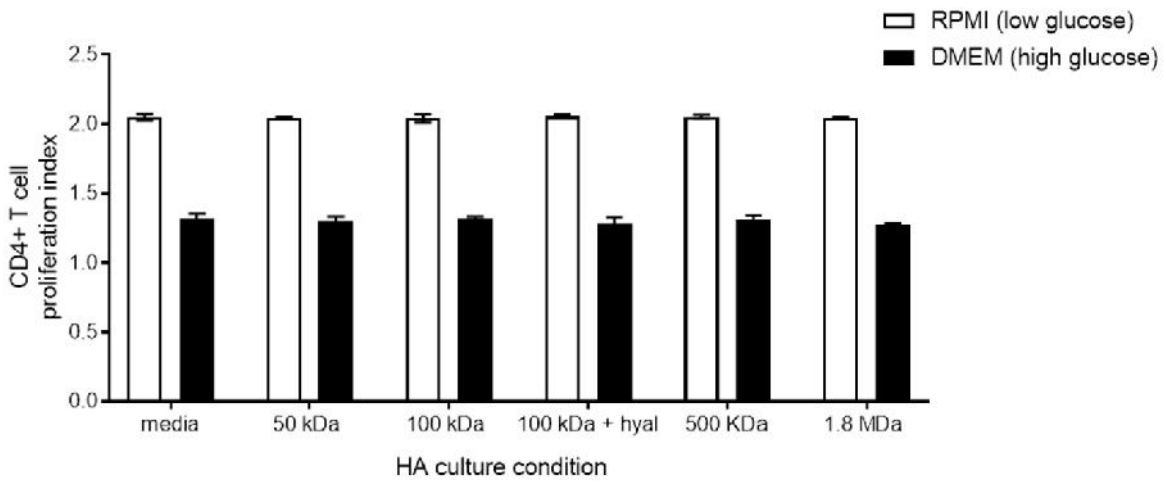


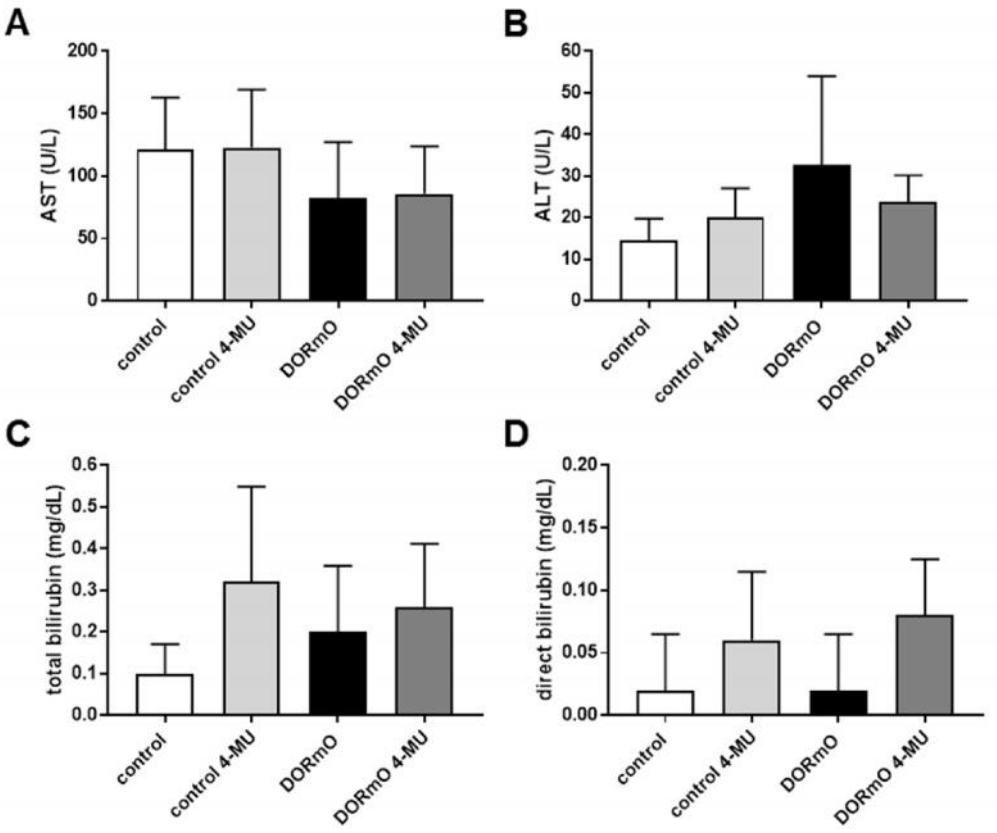
Supplemental Figure 1. Islet changes in young DORmO mice. A,C,E,G. Representative histologic staining of glucagon (A), F4/80 (C) cleaved caspase-3 (E) and CD44 (G) in pancreas tissue from control and DORmO mice fed 4-MU chow or control chow, shown in brown. Arrowheads show the apoptotic cells in the cleaved caspase-3 staining. B, D, F, H. Average islet area positive for glucagon (B), F4/80 (D) caspase-3 (F) and CD44 (H) staining, evaluated from histologic staining of pancreas tissue from control and DORmO mice. Bars show mean ± SEM; *, $p<0.05$ vs. control by unpaired t test.



Supplemental Figure 2. HYAL2 is increased in isolated DORmO islets. A,B. Relative mRNA expression of HYAL1 (A) and HYAL2 (B) from isolated islets of 8 week old control and DORmO mice. C. *In vitro* ROS measurement in INS-1 cells with and without 24 hour 4-MU treatment. Bars show mean ± SEM; *, $p<0.05$ vs. control by unpaired t test.



Supplemental Figure 3. HA size does not affect T cell proliferation. CD4+ T cell proliferation assay with HA sizes from 50 kDa to 1.8 MDa in DMEM (high glucose) and RPMI (low glucose) media to reflect diabetic and non-diabetic conditions. Additionally the 100 kDa HA was hyaluronidase digested (the fourth set of columns), hyaluronidase was given at the same time the HA was added. Bars show mean ± SEM.



Supplemental Figure 4. 4-MU does not affect liver function in mice. Liver function of control and DORmO mice with and without 4-MU treatment was measured in the serum. Mice were treated with 4-MU for 6 weeks. The liver panel included AST (A), ALT (B), total bilirubin (C) and direct bilirubin (D). N = 5 animals per group. Bars show mean ± SEM.