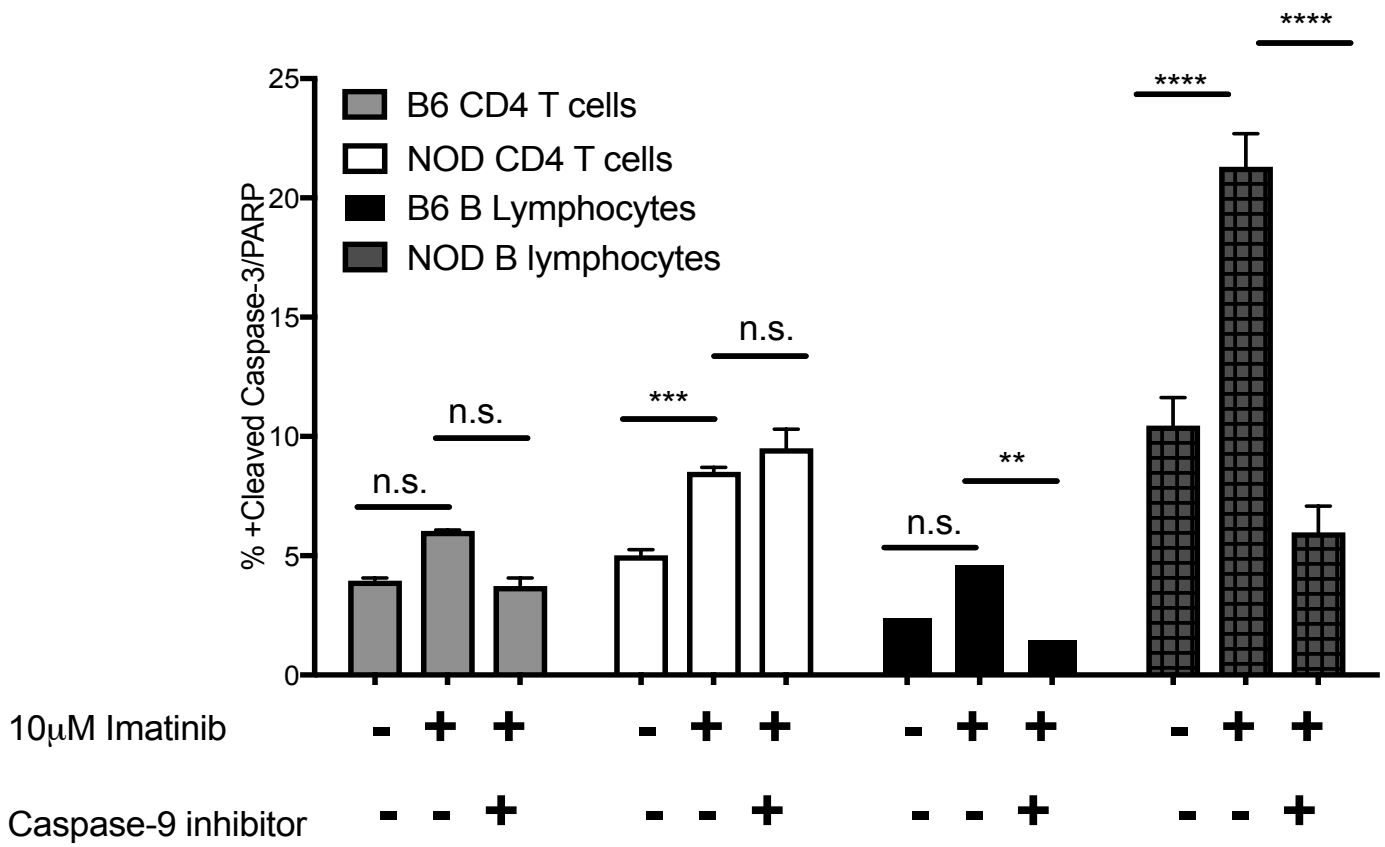
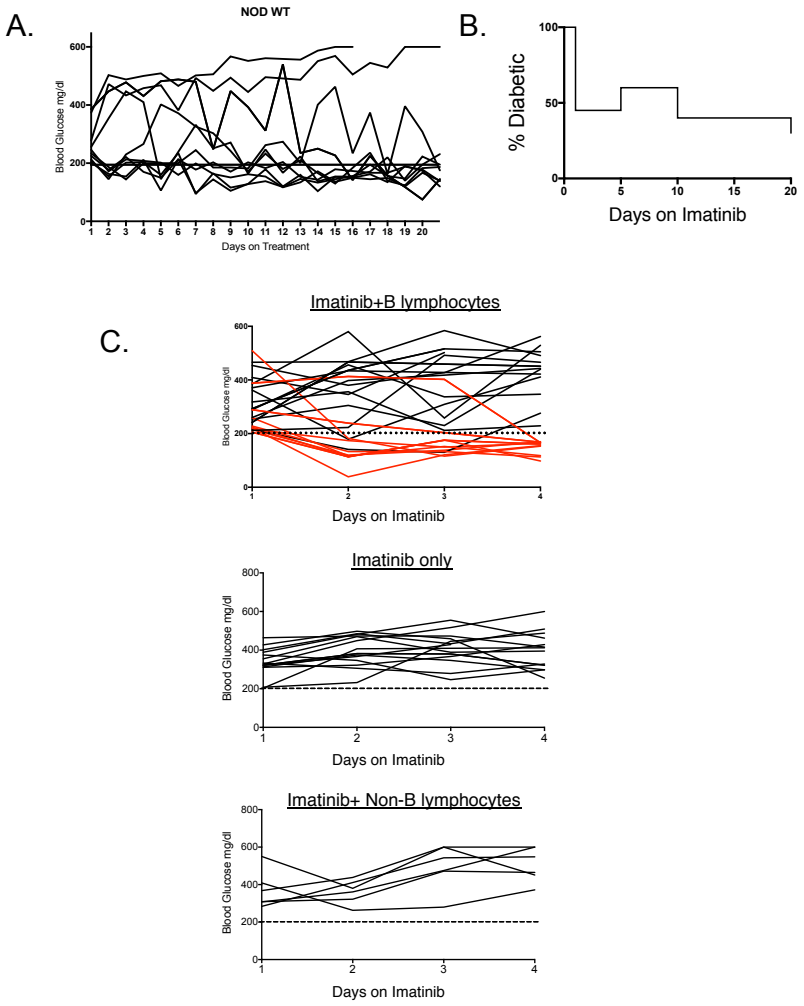
Supplemental 1:



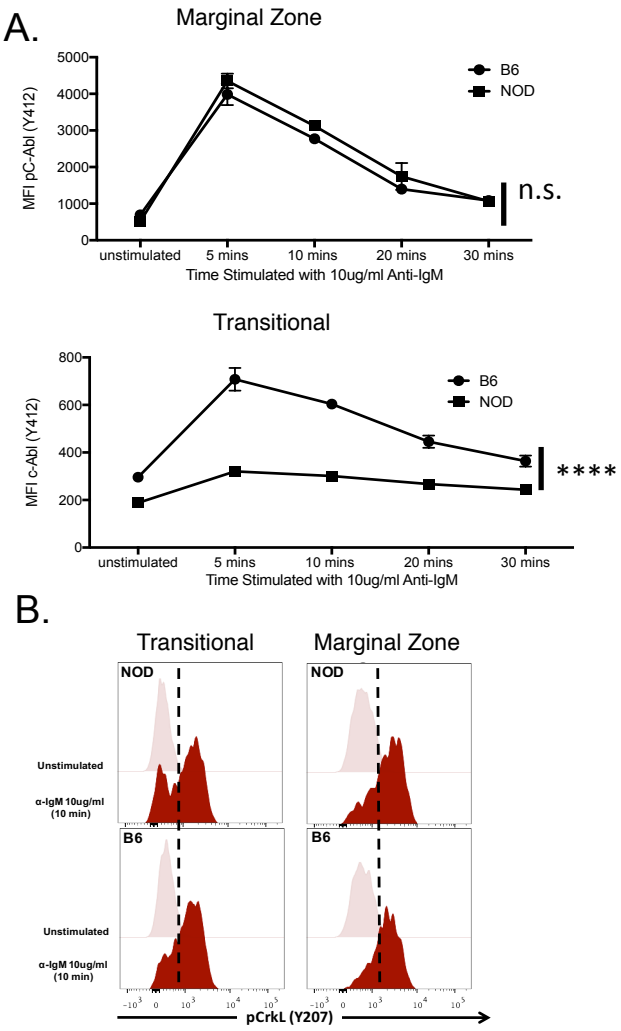
Supplemental Figure 1. NOD B lymphocytes preferentially undergo apoptosis in response to imatinib ex vivo. A) Total splenocytes were plated in DMEM supplemented with 10% FCS and Pen/Strep. Imatinib was added to these cells to a final concentration of 10uM. Apoptosis was analyzed by co-staining of cleaved-PARP and caspase-3. B lymphocytes from NOD mice demonstrated enhanced sensitivity to imatinib-induced apoptosis. Imatinib-induced apoptosis was reduced by Caspase-9 inhibitor (Z-LEHD-FMK). ****, $p < 0.0001$; ***, $p < 0.0003$; **, $p < 0.008$; n.s. = not significant (two-way ANOVA followed by Sidak's multiple comparisons test. representative of at least 3 experimental repeats)

Supplemental 2:



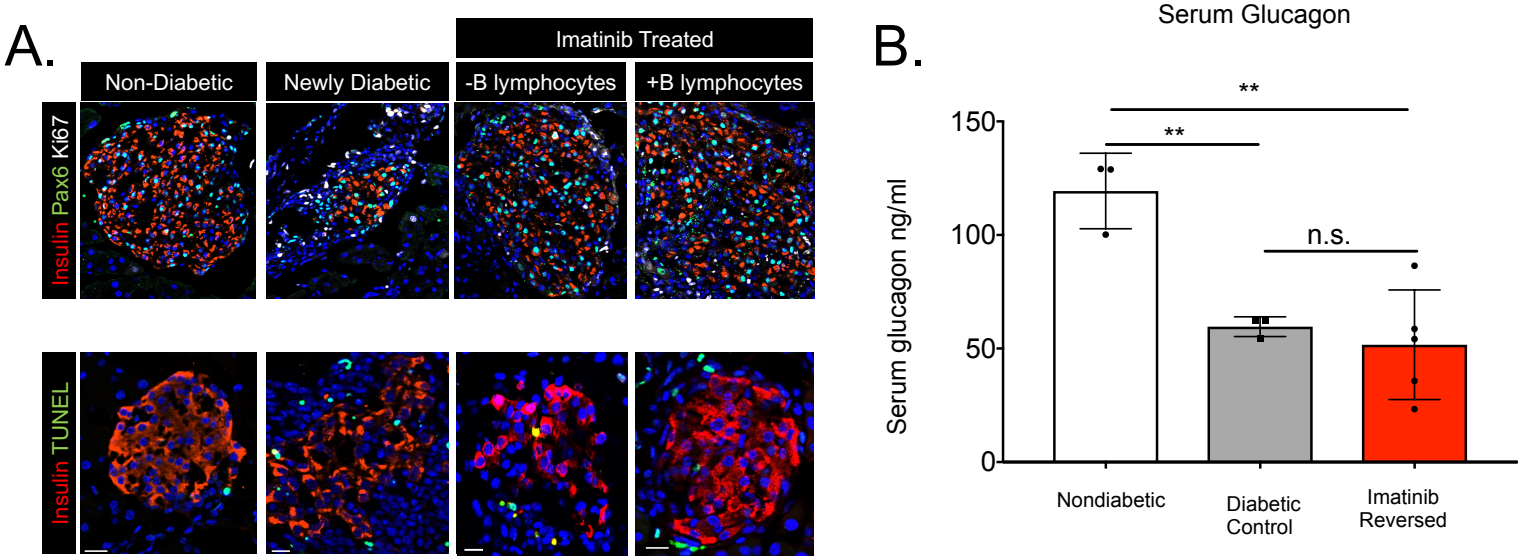
Supplemental Figure 2. Intraperitoneal imatinib mesylate injection reverses type 1 diabetes in NOD B cell sufficient mice. A) To test the efficacy of imatinib mesylate i.p. injection in reversal of diabetes in WT NOD, we allowed NOD mice to become diabetic. These mice were given 1.5mg of imatinib in saline for 21 days. At the end of this trial ~67% of mice had normal blood glucose levels (< 200mg/dL) (n=11). B) Analysis revealed that greater than 50% of NOD WT mice enrolled in imatinib reversal returned to normoglycemia by 3 weeks with nearly all responding mice improved by day 4. C) Individual blood glucose measurements of each cohort of NOD.Rag$^{-/-}$ mice. The blood glucose threshold for enrollment is indicated by the dotted line on each graph. Those mice that were scored as reversed at the end of the study are colored red. Only the group that received B lymphocytes and imatinib demonstrated return to euglycemia

Supplemental 3:



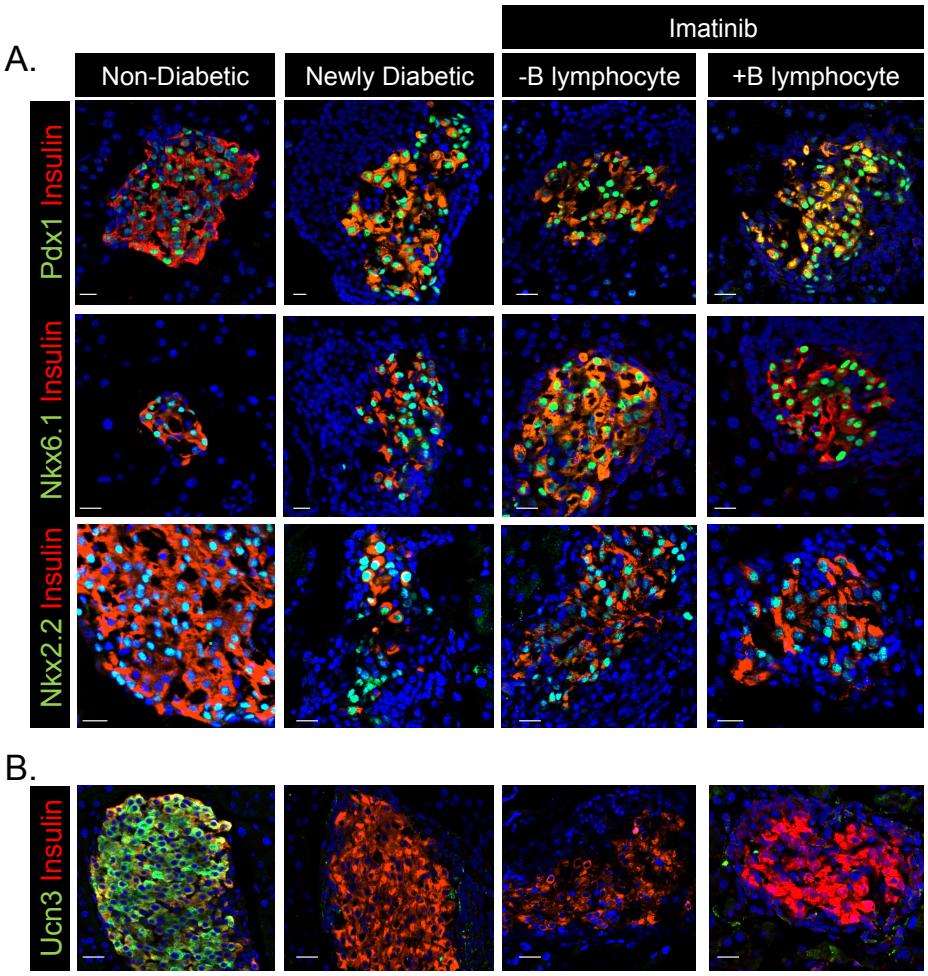
Supplemental Figure 3. NOD transitional B lymphocytes have reduced signaling c-Abl capacity. A) Quantification of the signaling capacity of marginal zone and transitional zone B lymphocytes from NOD mice reveals that only transitional B lymphocytes have reduced signaling capacity in NOD mice as compared to B6. (n=3 and is representative of at least 10 experimental repeats) B) This reduction in c-Abl signaling was linked to downstream reduction in signaling in c-Abl target Crkl phosphorylation (Y207) in transitional but not marginal zone B lymphocytes. ****, $p < 0.001$; n.s. = not significant. (One-way ANOVA. representative of at least 7 experimental repeats)

Supplemental 4:

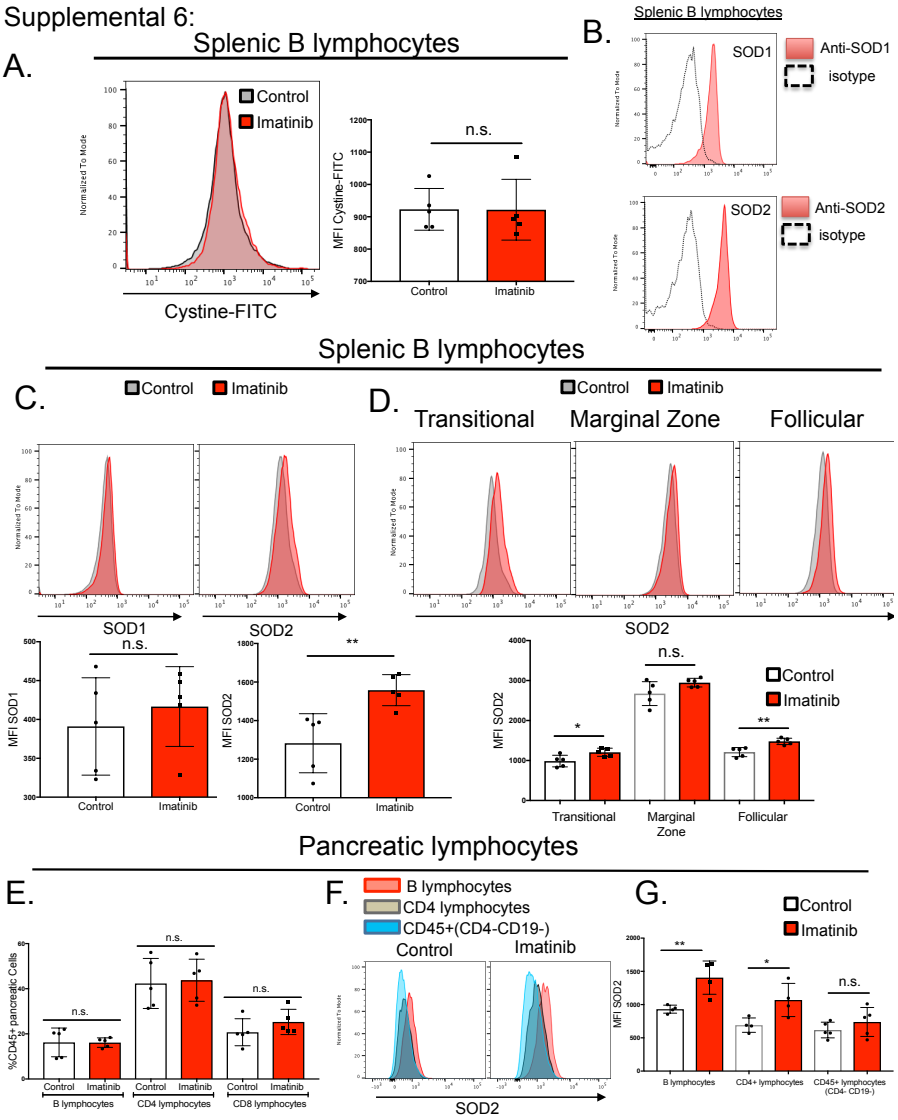


Supplemental Figure 4. There is no difference in Pax6, proliferation apoptosis, or glucagon levels in diabetic or imatinib-treated mice. A) Pancreatic sections stained with Pax6 (endocrine), insulin, and Ki67 revealed no enhanced islet cell proliferation. Sections subjected to TUNEL assays revealed no enhanced islet apoptosis among any of the groups. (n=3 in each group). B) Serum glucagon levels in non-diabetic, diabetic controls and imatinib-reversed NOD mice revealed loss of glucagon between nondiabetic controls and both imatinib treated and diabetic mice (**p=0.0038 two-way ANOVA followed by Sidak's multiple comparisons test). The amount of secreted glucagon was not increased in NOD WT mice treated with imatinib.

Supplemental Figure 5:



Supplemental Figure 5. There is no change in Pdx1, Nkx6.1, or Nkx2.2 in diabetic or imatinib-treated mice. A) Staining of insulin and transcription factors Pdx1, Nkx6.1 and Nkx2.2 revealed no differences in any group assessed. B) Urocortin 3 (Ucn3), a secreted factor from beta cells that regulates somatostatin release from neighboring delta cells, was not restored in beta cells following diabetes reversal by imatinib. (representative data from 3 mice)



Supplemental Figure 6. Imatinib treated B lymphocytes have enhanced antioxidant capacity potential. A) Cystine uptake is an indication of increased activity of the glutathione peroxidase system. We noted no increase in cystine uptake as measured by flow cytometry in imatinib-treated B lymphocytes. (n.s. = not significant (n=5)) B) Splenic B lymphocytes from imatinib-treated NOD mice and untreated NOD controls were fixed, permeabilized and stained for intracellular SOD1(Cu-Zn) and SOD2 (MnSOD). These stains indicate the antibodies we utilized possessed specificity for SOD1 and SOD2 over isotype controls in NOD B lymphocytes. C) There was no increase in SOD1 but SOD2 expression did increase as measured by flow cytometry (** p = 0.0026 Student's t-test). D) Marginal zone B lymphocytes possessed the highest levels of SOD2 and did not increase SOD2 after imatinib. Transitional and follicular B lymphocytes persisting after imatinib therapy also increased SOD2 expression (* p = 0.024 and ** p = 0.0075 respectively two-way ANOVA followed by Sidak's multiple comparisons test) **(**n=5 in each group and is representative of at least 4 repeats) E) Flow cytometry analysis revealed no changes in the proportions of B, CD4 or CD8 lymphocytes in the pancreas. (n=5 two-way ANOVA followed by Sidak's multiple comparisons test) F) B lymphocytes were isolated from the pancreas of imatinib-treated and untreated control NOD mice. SOD2 expression is increased in these lymphocytes (* p = 0.013 **p=0.0083 Student's T-test). G) B lymphocytes expressed the highest level of SOD2 of all CD45+ lymphocytes at baseline and in response to imatinib **(**n=4 in each group). Data representative of at least 3 experimental repeats.