**Supplementary Figure 1.** Ngn3-Btc+PD-L1 induces neo-islets in the periportal regions of the liver. (A) Representative sections of Ngn3-Btc+PD-L1 treated diabetic NOD mouse liver stained by immunohistochemistry for insulin; C-peptide; glucagon; somatostatin (SST); pancreatic polypeptide (PP) at indicated time points after treatment. Periportal neo-islets are shown encircled by the red line. (B-C) Insulin staining in the pancreas with lower (C) and higher (D) magnifications of a neo-islet is indicated by the red arrow in (B). Scale bar represents 20μm in (A), 100μm in (B) and 50μm in (C). PV-Portal vein.
Supplementary Figure 2. PD-L1 and PD-L2 expression level in the liver or pancreas of Ngn3-Btc and Ngn3-Btc+PD-L1 treated NOD mice. (A) PD-L1 staining in the liver or pancreas of Ngn3-Btc and Ngn3-Btc+PD-L1 treated NOD mice. (B) PD-L1 and PD-L2 RNA level in the liver of Ngn3-Btc and Ngn3-Btc+PD-L1 treated NOD mice. Scale bar represents 20 μm.
Supplementary Figure 3. Neo-islets express islet hormones and transcription factors. RT-qPCR showing the expression of (A) islet hormones and (B-C) transcription factors involved in islet development at 4 weeks and non diabetic and diabetic NOD control mice. n=4-5, all values are mean±SEM; * p≤0.05.
SUPPLEMENTARY DATA

Supplementary Figure 4. Neo-islets induced by Ngn3-Btc+PD-L1 in the liver expresses the hepatic oval cell marker. (A) A6 staining. (B) OC2-1D11 and CD3 staining in different groups. Scale bar represents 20μm.
Supplementary Figure 5. There is no difference in the number of CD4+ and CD8+ cells in the whole liver of Ngn3-Btc and Ngn3-Btc+PD-L1 treated mice. Representative dot plot of CD4+ (A) and CD8+ (C) T cells among CD3+ T cells in whole liver treated with Ngn3-Btc or Ngn3-Btc+PD-L1. (B,D) Percentage of CD4+ (D) and CD8+ (F) among CD3+ T cells in whole liver. All values are mean±SEM; * p≤0.05. n=4-5 for each group. Scale bar represents 50μm.
SUPPLEMENTARY DATA

Supplementary Figure 6. There is no difference in the number of Foxp3+ in the whole liver or in the periportal regions of the liver of Ngn3-Btc and Ngn3-Btc+PD-L1 treated mice. (A) Representative dot plot of Foxp3+ among CD4+ T cells in whole liver treated with Ngn3-Btc or Ngn3-Btc+PD-L1. (B) Percentage of Foxp3+ among CD4+ T cells in whole liver. (C–D) Western Blot from the whole liver also shows no change of Foxp3 expression in the liver of different treated groups. (E) The quantitation for counting the number of Foxp3+ among CD4+ T-cells in the periportal clusters in different treated groups N=4-5/group. All values are mean±SEM.
Supplementary Figure 7. Neo-islets do not express MHCII antigens. (A) MHCII staining does not co-localize with c-peptide staining in neo-islets. (B) B220 (B cell marker) positive cells and CD4 positive cells are both present infiltrating the periportal neo-islet. (C) MHCII is expressed in the B220 positive B lymphocytes in the periportal area. Scale bar represents 50μm.
Supplementary Figure 8. TNF-α and IFN-γ production in CD4 lymphocytes in different tissues of recent onset diabetic NOD mice. Representative dot plot and quantitation of IFN-γ production (A,C) and TNF-α (B,D) in the spleen, pancreas, pancreas lymph node and mesentery lymph node of diabetic NOD mice. Control shown is unstimulated CD4+ T-cells from the spleen of untreated NOD mice. C & D represent the quantification from 3 separate mice in the group.
**Supplementary Figure 9.** Virus clearance shows no immunosuppression in the mice treated with Ngn3-Btc+PDL1. (A) 1*10^11 helper virus was iv injected to Ngn3-Btc and Ngn3-Btc+PD-L1 treated mice for 3d and 3w. Q-PCR shows relative virus clearance in different mice. N=2-3/group.