Supplementary Fig 1. Heatmap analysis of microarray samples using $T_{FH}$, Th1, Th2 or Th17 signature genes. Heatmap analysis showing hierarchical clustering of Treg or T cell samples isolated from the pancreatic LN or inguinal LN of 6 week old DO11 x rip-mOVA mice (as in Figure 1) using selected signature genes of $T_{FH}$, Th1, Th2, or Th17 differentiation. Additional heatmaps show the gene expression changes associated with activation of conventional T cells in vitro using anti-CD3 and anti-CD28 antibodies. Note that many "Th1" or "Th2" genes can be induced by activation implying their upregulation could reflect activation rather necessarily being indicative of the T cell differentiation state.
Supplementary Fig 2. Confocal analysis of Germinal Centers in the PanLN of DO11 x rip-mOVA mice. (A) Confocal images of frozen sections of PanLN and IngLN from an 18wk old DO11 x rip-mOVA mouse stained for Ki67 (green) CD3 (blue) and IgM (red). 2 germinal centers are visible in the PanLN. (B) Collated data showing the number of germinal centers detected in PanLN and IngLN of 11-18wk old DO11 x rip-mOVA and DO11 mice. (n=5) **P<0.01
Supplementary Fig 3. mRNA levels for CXCR-5, PD-1, ICOS and CCR9 in pancreas-infiltrating T cells. CD4 T cells were isolated by cell sorting from the pancreas or peripheral (inguinal) LN of 11-18wk old DO11 x rip-mOVA mice and mRNA levels of the indicated molecules were assessed. Columns show the mean of 5 data points, each of which derives from material pooled from 3-8 mice. P values are indicated.
Supplementary Fig 4. Relationship between CXCR5% and clinical features. Correlation between the frequency of CXCR5+ cells within total CD4 cells (A) and within central memory CD4 cells (B) with patient age, disease duration, blood glucose levels at the time of blood draw and Haemoglobin A1c (A1C) in patients with Type 1 Diabetes. (C) Frequencies of CD4+CXCR5+ T cells that co-express CCR6 and/or CXCR3 in patients with Type 1 Diabetes (n=19) and healthy controls (n=13) (improved ICOS staining was achieved by use of ICOS biotin and streptavidin APC). Bars show mean and standard error (P=NS).
**Supplementary Fig 5.** An independent cohort of Type 1 Diabetes patients and healthy controls was analysed 2 years after the data presented in Figure 6 was collected. (A) Frequencies of CXCR5+ cells or CXCR5+ICOS+ cells within peripheral blood CD3+CD4+ cells are shown (T1D, n=17; Con, n=13). Box and whisker plots show the median, interquartile range and 10th-90th percentile. (B) Frequencies of CXCR5+ cells and CXCR5+ICOS+ cells within peripheral blood CD3+CD4+ cells from only those individuals positive for DR3 and/or DR4 (T1D, n=6; Con, n=8). Box and whisker plots show the median, interquartile range and 10th-90th percentile. (C) HLA class II DRB1 and DQB1 typing for available samples in this cohort. Allele type and frequency is shown. Autoantibody status is indicated in the Patient Table (GAD, IA-2, ZnT8R and ZnT8W). Blank cells indicate readings below threshold levels. There was not a significant difference between the frequency of CXCR5+ or CXCR5+ICOS+ T cells between autoantibody+ and autoantibody- individuals.
Supplementary Fig 6. Example stains and gating strategy for the pSTAT5 assay. Gated CD3+CD4+ T cells were divided into conventional T cells and Treg on the basis of CD127+ and Foxp3+ staining. Naive T cells were identified on the basis of CD45RA staining. pSTAT5 staining in the absence and presence of 100ng/ml IL-2 is shown.
**Supplementary Fig 7.** Visual representation of how each individual patient sample was used for the assays presented in this study. Table showing which patients were used for each of the data figures presented in the manuscript.