**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.
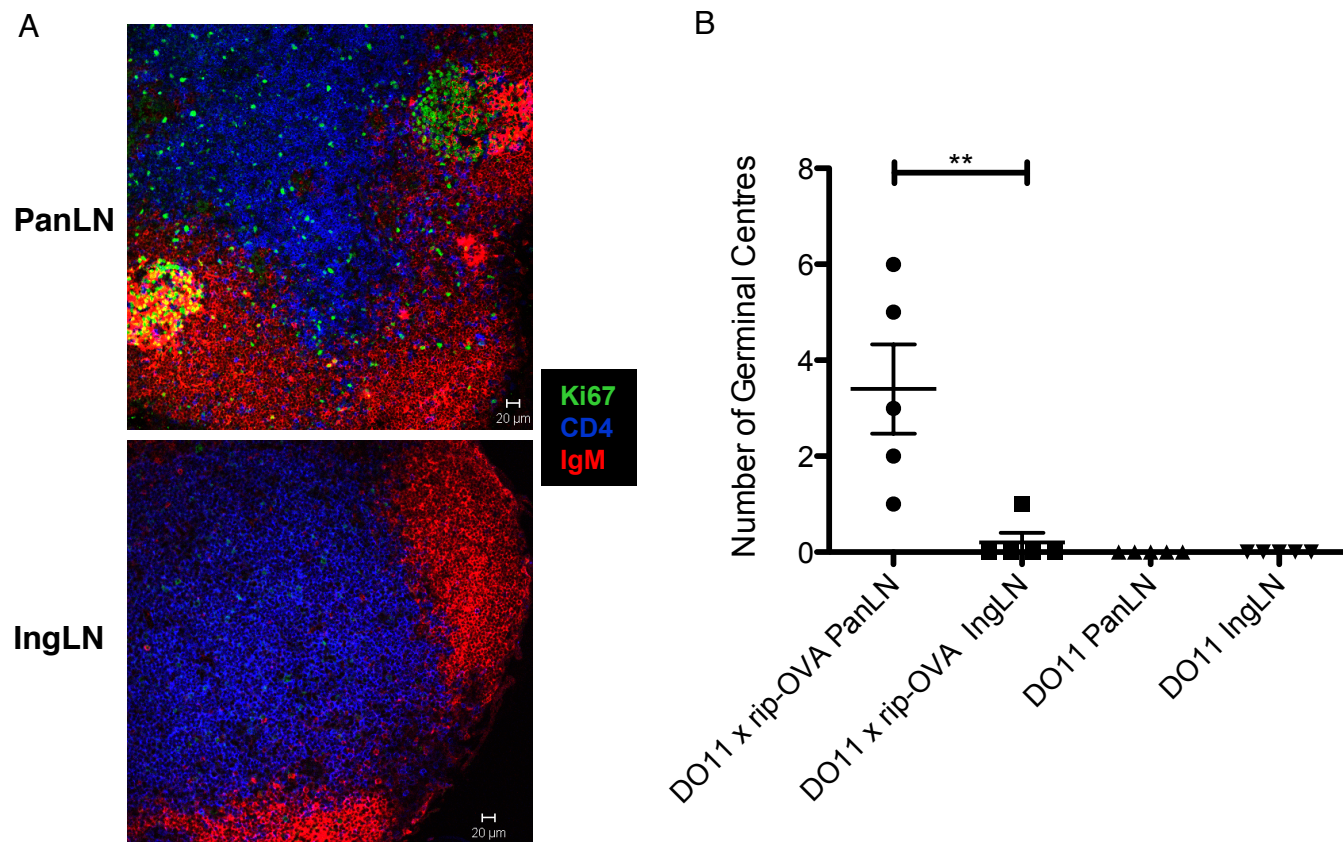
Supplementary Fig 2. Confocal analysis of Germinal Centers in the PanLN of DO11 x rip-mOVA mice. (**A**) Confocal images of frozen sections of PanLN and IngLN from an 18wk old DO11 x rip-mOVA mouse stained for Ki67 (green) CD3 (blue) and IgM (red). 2 germinal centers are visible in the PanLN. (**B**) 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
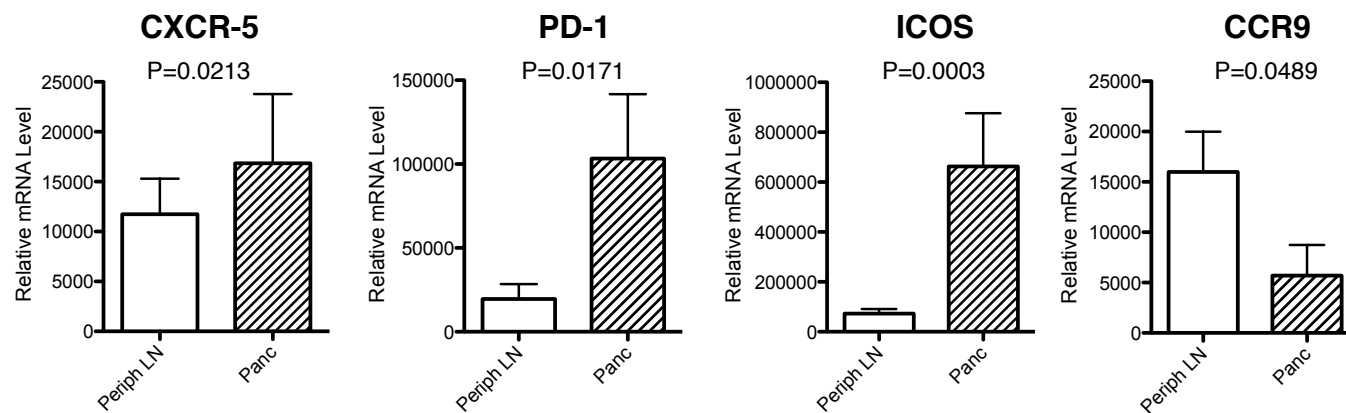
**Supplementary Fig 3.** mRNA levels for CXCR-5, PD-1, ICOS and CCR9 in pancreas-infiltrating T cells. CD4 T cells were isolated by cell sorting from the pancreas or peripheral (inguinal) LN of 11-18wk old DO11 x rip-mOVA mice and mRNA levels of the indicated molecules were assessed. Columns show the mean of 5 data points, each of which derives from material pooled from 3-8 mice. P values are indicated.
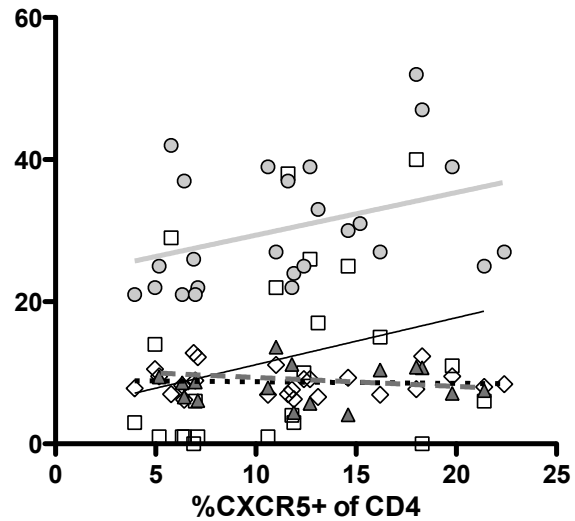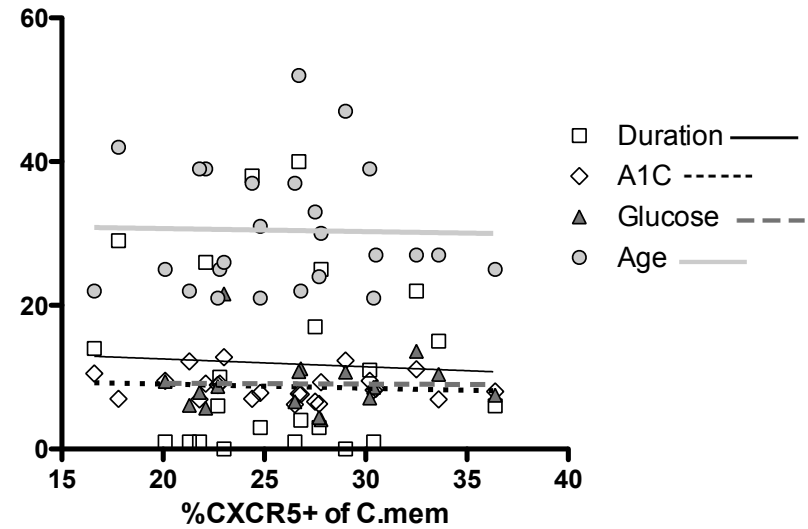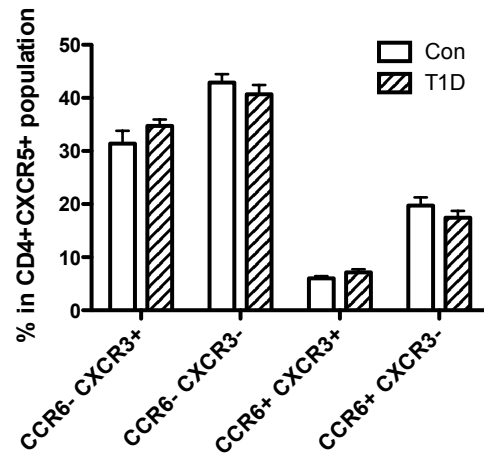
Supplementary Fig 4. Relationship between CXCR5% and clinical features. Correlation between the frequency of CXCR5+ cells within total CD4 cells (**A**) and within central memory CD4 cells (**B**) with patient age, disease duration, blood glucose levels at the time of blood draw and Haemoglobin A1c (A1C) 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).

A

P= 0.0025

%CXCR5+ ICOS+

Con T1D

P= 0.0069

%CXCR5+

Con T1D

B

P= 0.0180

CXCR5+ICOS+

Con DR3/4 T1D DR3/4

P= 0.0392

CXCR5+

Con DR3/4 T1D DR3/4

C

Patients				
DR allele 1	DR allele 2	DQB allele 1	DQB allele 2	Auto-antibodies
03	11	0301	04	GAD
07	15	02	0602	GAD
13	07	0303	0604	GAD, IA-2, ZnT8R
07	07	02	0303	
07	13	0502	0303	
15	07	04	0501	
07	15	02	?	GAD
03	15	0201	0602	GAD
03	04	0201	0301	
01	03	0201	0301	
10	15	0501	0502	GAD
03	04	0201	0302	
03	04	0201	0301	

Controls			
DR allele 1	DR allele 2	DQB allele 1	DQB allele 2
03	07	0201	02
07	13	02	0301
01	16	0501	0502
03	15	0201	0601
04	11	0301	0301
03	07	0201	0303
03	13	0201	0604
04	14	0302	0503
01	03	0501	0201
01	14	0501	0503
03	07	0201	0303
01	07	0501	0303

Allele Frequency

Con T1D

DR03 DR04 DR07 DR10 DR15 DR13 DR16

Allele Frequency

Con T1D

DQ0301 DQ02 DQ0201 DQ04 DQ0501 DQ0502 DQ0602 DQ0604 DQ0303

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.
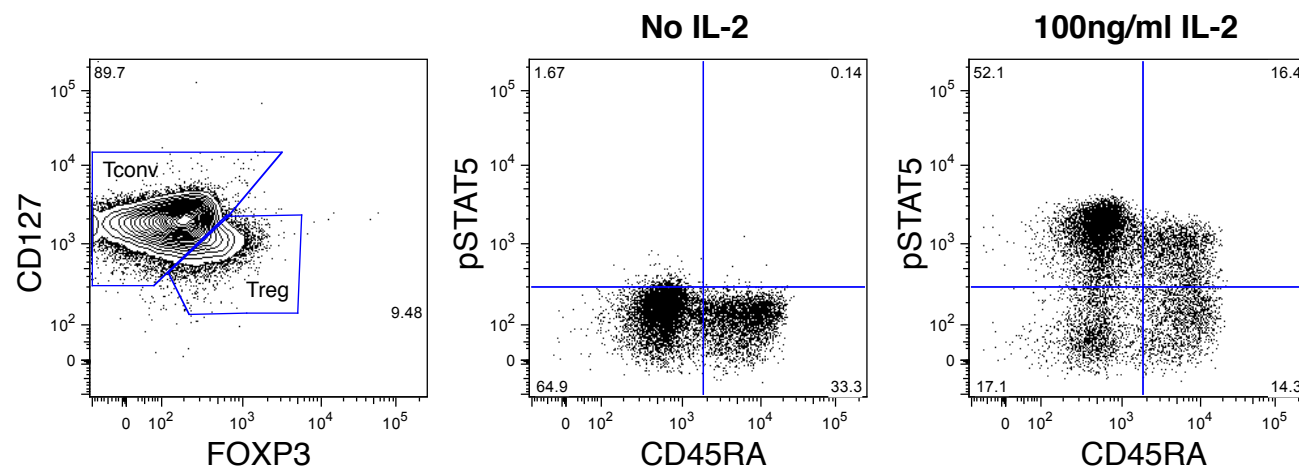
Supplementary Fig 6. Example stains and gating strategy for the pSTAT5 assay. Gated CD3+CD4+ T cells were divided into conventional T cells and Treg on the basis of CD127+ and Foxp3+ staining. Naïve T cells were identified on the basis of CD45RA staining. pSTAT5 staining in the absence and presence of 100ng/ml IL-2 is shown.

Patient Number 1–51

Patient Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51
Realtime PCR (Fig 3)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																																	
Tfh (Fig 4)																			x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x					
Cytokine (Fig 5)	x	x	x	x								x	x	x	x													x											x	x	x			x	x	x	x	x	x	x	x
IL-21/Tfh (Fig 5D)														x	x													x											x	x				x	x	x	x	x	x	x	x
Clinical Correlations (Sup 4A,B)																			x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x					

Patient Number 52–102

Patient Number	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102
CXCR5 upregulation (Fig 6A,B)																								x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
pSTAT Data (Fig 6c)																																						x	x	x	x	x	x	x	x	x	x	x	x	x	x
CCR6/CXCR3 (Sup 4C)	x	x	x	x	x	x	x	x	x	x								x	x	x	x	x	x																												
Tfh (Sup 5)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																																		

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.