

**Supplemental Table 1. Information on healthy donors (HD) used for this study**

<b>Subject ID</b>	<b>Age<sup>a</sup></b>	<b>Gender<sup>b</sup></b>	<b>PTPN22 SNP<sup>c</sup></b>
HD #1	33	F	C/C
HD #2	42	F	C/C
HD #3	42	F	C/C
HD #4	30	F	C/C
HD #5	40	M	C/C
HD #6	24	F	C/C
HD #7	27	M	C/C
HD #8	35	F	C/C
HD #9	40	F	C/C
HD #10	42	F	C/C
HD #11	26	M	N/D <sup>d</sup>
HD #12	43	M	N/D

<sup>a</sup> The mean age was 35.3 years.

<sup>b</sup> The female to male ratio was 4:1.

<sup>c</sup> Denotes single nucleotide polymorphism (SNP) identified by genotyping PTPN22 at position 1858.

<sup>d</sup> Not determined.

**Supplemental Table 2. Information on type 1 diabetic subjects used for study**

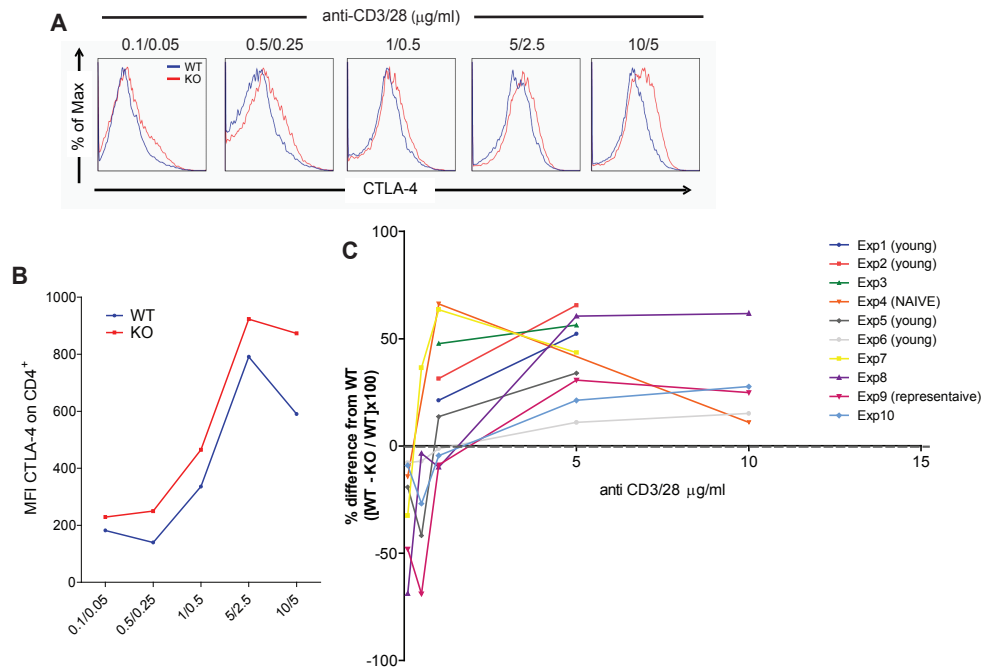
<b>Subject</b>	<b>Age<sup>a</sup></b>	<b>Gender<sup>b</sup></b>	<b>Time since</b>	<b>PTPN22 SNP<sup>d</sup></b>
T1D #1	43	M	25 years	C/C
T1D #2	53	F	42 years	C/C
T1D #3	43	F	35 years	C/C
T1D #4	27	F	12 years	C/C
T1D #5	43	M	25 years	C/C
T1D #6	41	F	12 years	C/C
T1D #7	56	M	13 years	C/C

<sup>a</sup> The mean age was 43.7 years.

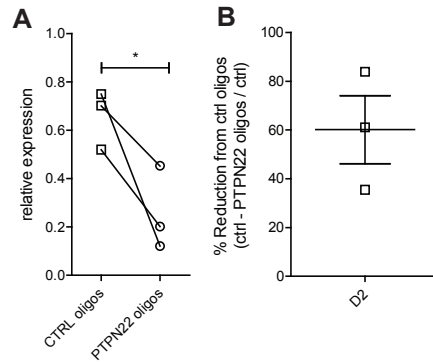
<sup>b</sup> The average time since diagnosis was 23.4 years.

<sup>c</sup> The female to male ratio was 4:3.

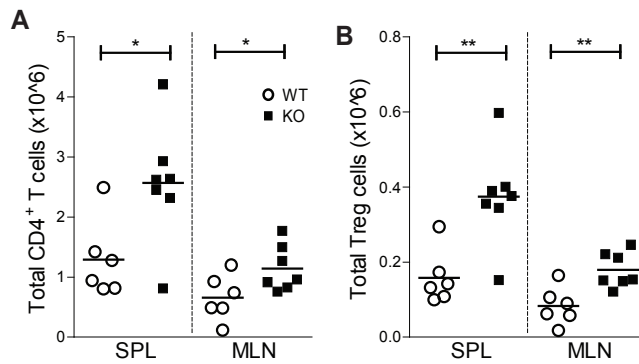
<sup>d</sup> Denotes single nucleotide polymorphism (SNP) identified by genotyping PTPN22 at position 1858.



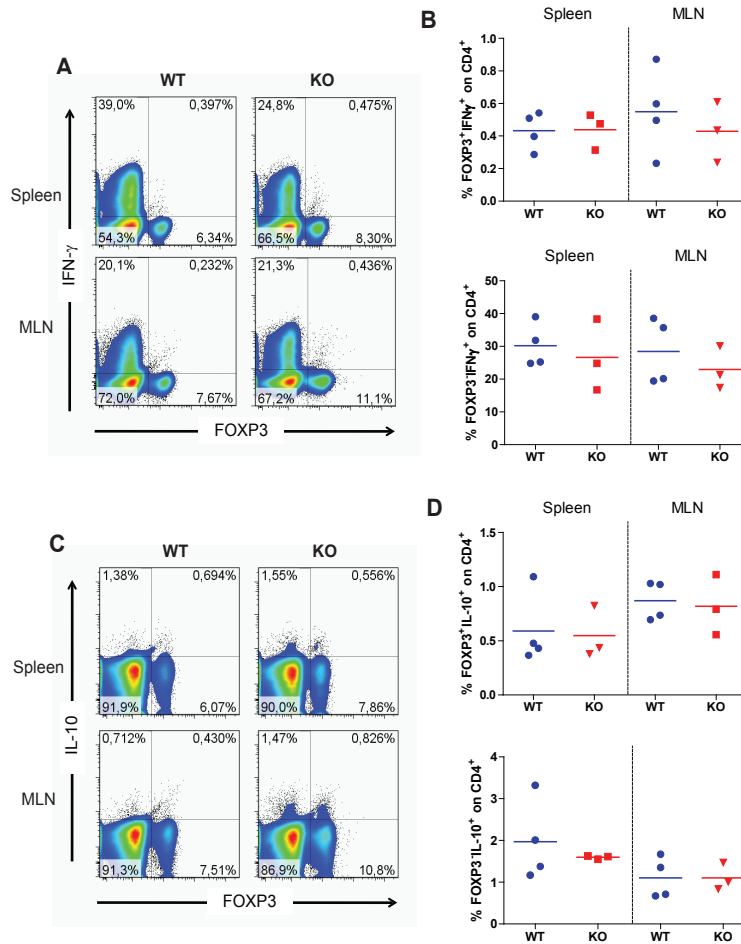
**Supplementary Figure 1.** PTPN22 affects FOXP3 induction by inhibiting T cell activation in mice. CD4<sup>+</sup>CD25<sup>-</sup> T cells from 8-12 wk-old wild-type (WT) or PTPN22.KO mice were cultured under iTreg polarizing conditions with increasing amounts of anti-CD3/CD28 mAbs. (A) Histogram overlay depicting the levels of CTLA-4 in WT and PTPN22.KO CD4<sup>+</sup> T cells 4 days after culture. Blue line indicates WT cells, whereas red, KO. (B) The MFI levels of CTLA-4 in WT and KO cells depicted in C shown in a graph. Results from one representative experiment are shown. (C) Cumulative data showing the % difference in CD25<sup>+</sup>FOXP3<sup>+</sup> induction between WT and KO cells from ten independent experiments are displayed in a graph. Each colored line indicates results from independent experiments. In some experiments, naive T cells (CD4<sup>+</sup>CD62L<sup>hi</sup>) or cells from young animals (>6 wks-old) were cultured (indicated in the figure, including the experiment that was selected as representative in Fig.1). Not all anti-CD3/28 activating conditions were tested in each experiment.



**Supplementary Figure 2.** Antisense PTPN22-specific oligonucleotide treatment reduces by 50% the endogenous PTPN22 expression levels in human iTreg cultures. (A) Human CD4+CD127+CD25- T cells from HD were FACS-sorted and cultured under iTreg polarizing conditions as described in Materials and Methods. PTPN22-specific and control (CTRL) oligonucleotides were added at the beginning of iTreg cultures with CD4+ T cells derived from HD. Expression levels of PTPN22 were evaluated 2 days later by real-time qPCR,  $p < 0.05$ . (B) Percent reduction of PTPN22 expression levels in human CD4+ T cells as compared to CTRL oligos. Each open square represents individual donor.



**Supplementary Figure 3.** CD4 T cell expansion and Treg cell development upon lymphopenic expansion in the absence of PTPN22. (A-B) Forty five days after transfer into lymphopenic B6.Rag1<sup>-/-</sup> hosts, CD4<sup>+</sup>CD25<sup>-</sup> T cells from PTPN22 WT and PTPN22.KO mice were studied for expansion (total number of CD4<sup>+</sup> T cells) and iTreg conversion in the SPL and MLN. Each symbol represents individual animal and horizontal bar shows the mean of values. \*, p<0.05, \*\*,p<0.005.



**Supplementary Figure 4.** Cytokine production by peripherally-induced Treg and Teff in the absence of PTPN22. (A-B) Forty five days after transfer into lymphopenic B6.Rag1<sup>-/-</sup> hosts, CD4<sup>+</sup>CD25<sup>-</sup> cells from PTPN22.WT and PTPN22.KO mice converted into FOXP3-expressing pTregs and memory cells in the spleen and MLN. Total lymphocytes were activated with leukocyte activation cocktail (LAC) prior to staining intra-cytoplasmically for FOXP3 and IFN- $\gamma$  (A-B) or IL-10 (C-D) anti-cytokine antibodies. One representative experiment of two with similar results is shown in A and C after gating on total CD4<sup>+</sup> T cells. Each dot represents individual mice in B and D and horizontal bar shows the mean of values.