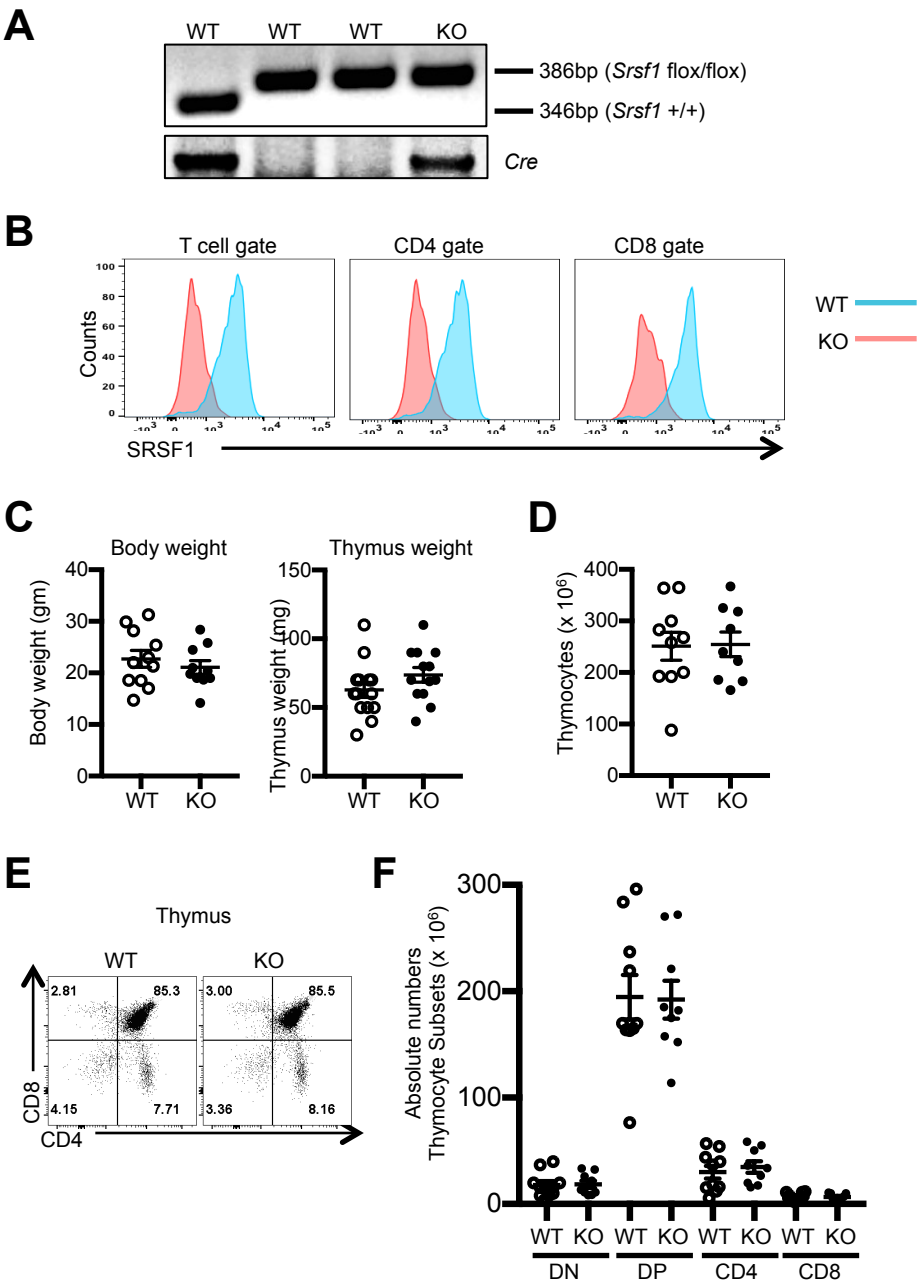
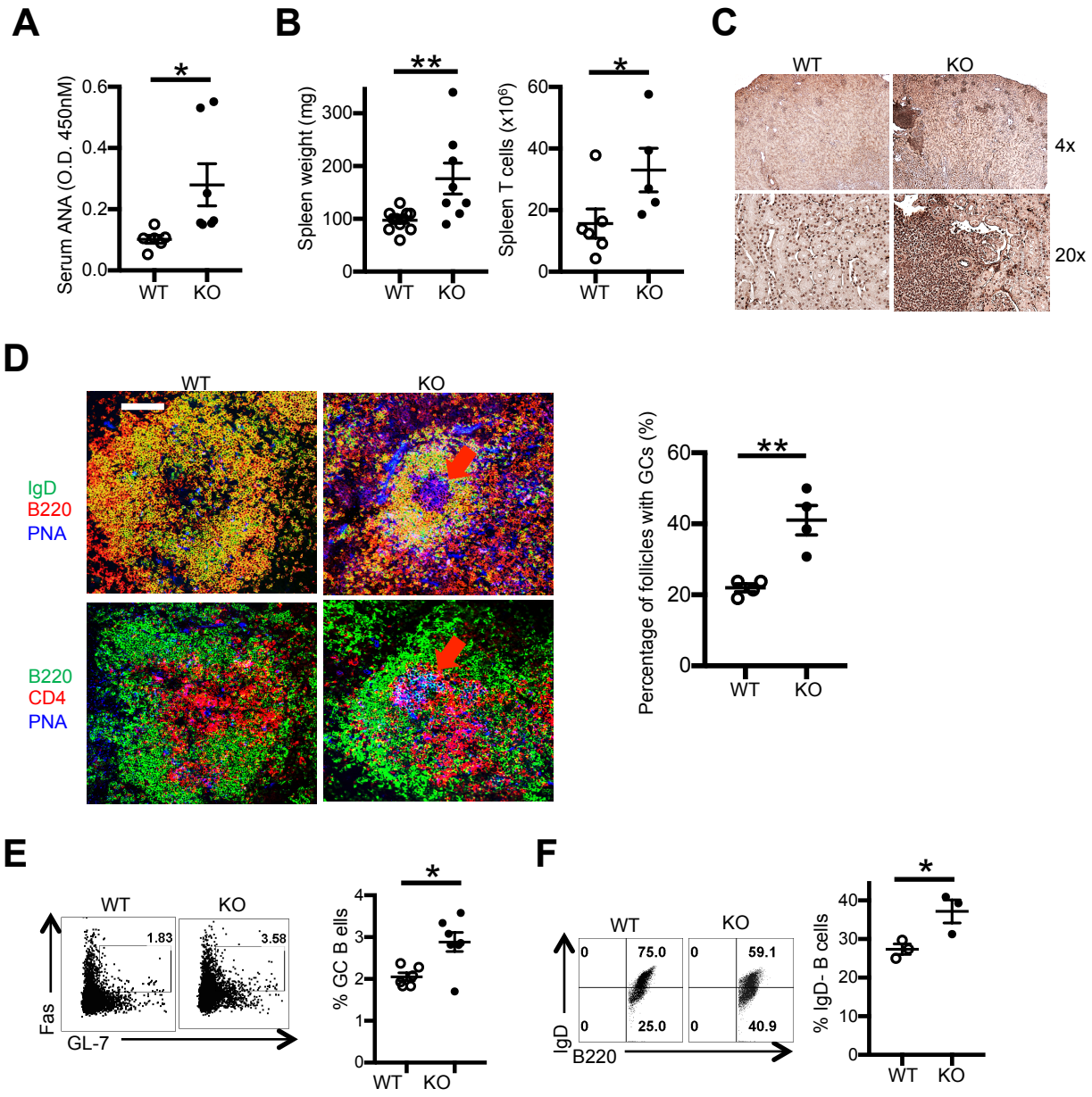
Supplemental Figure 1.



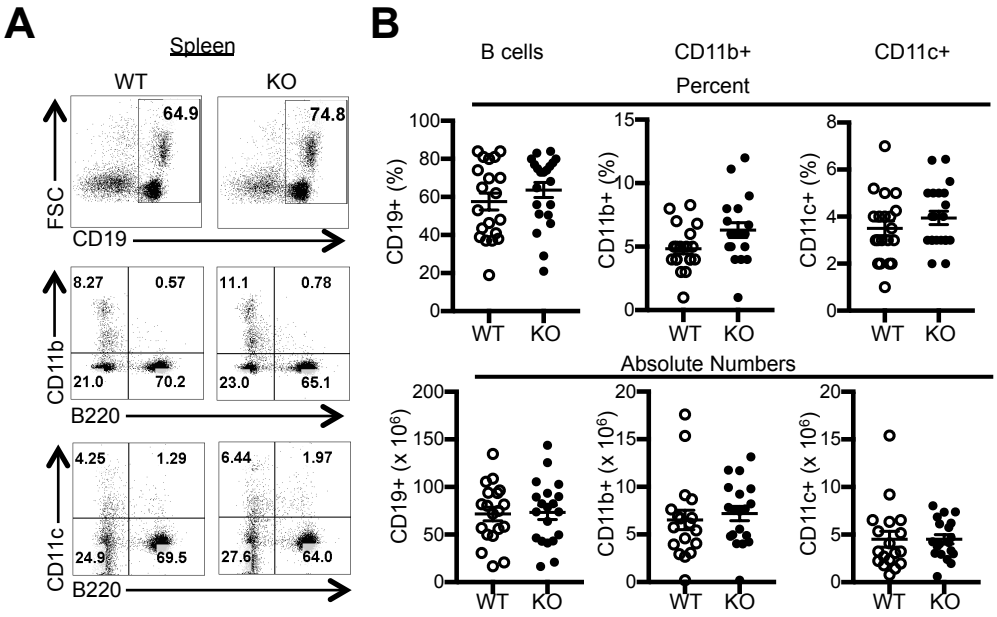
Supplemental Figure 1. Generation of *Srsf1*-cKO mice. (A) Tail genomic DNA was used for PCR amplification of *Srsf1*-flox and *dLck-Cre* genes. WT (*Srsf1* +/+ *Cre*+, or *Srsf1* flox/flox *Cre*-) and *Srsf1*-cKO (*Srsf1* flox/flox *Cre*+) mice are indicated. **(B)** Spleen cells were isolated from WT and *Srsf1*-cKO mice, surface stained for Thy1.2, TCRβ, CD4, CD8 and intracellular stained for SRSF1. Plots show SRSF1 staining gated on live T cells, CD4 and CD8 T cells. **(C)** Body weight and thymus weight of 4-14 week old mice (Body Weight: n= 11WT, 10KO, Thymus weight: n= 14WT, 13KO). **(D)** Cells were isolated from thymus and analyzed by flow cytometry. Graph shows thymus cell counts (n= 10WT, 9KO). **(E)** Flow cytometry plots show thymocyte populations gated on live Thy1.2+ cells. **(F)** Graph shows absolute numbers of DN, DP, and SP CD4 and CD8 T cells in thymus (n=10WT, 9KO).

Supplemental Figure 2.



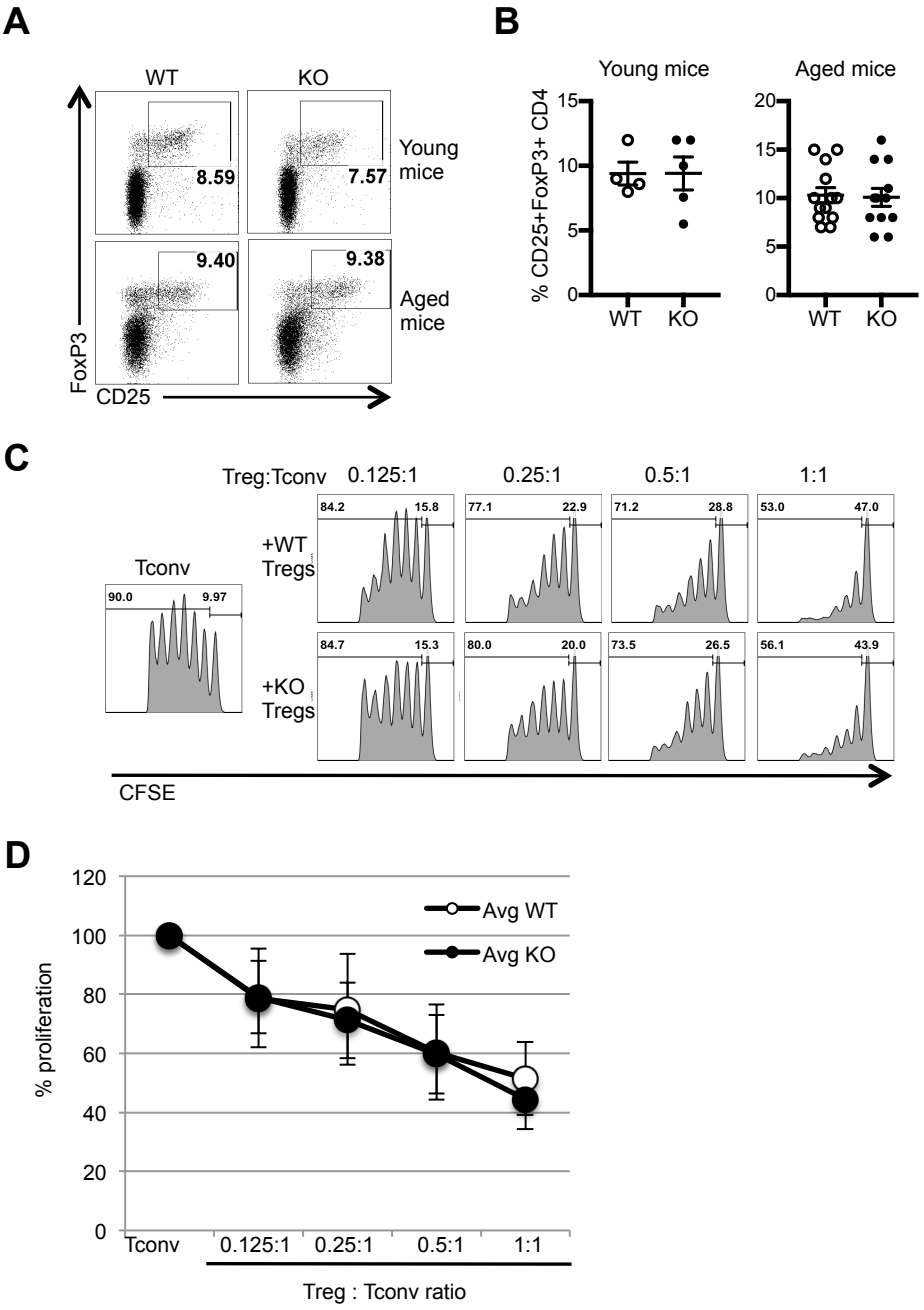
Supplemental Figure 2. *Srsf1*-cKO mice develop systemic autoimmune disease (A) Sera from WT and *Srsf1*-cKO mice (24 week-old) were analyzed for anti-nuclear antibodies (ANA) by ELISA (n= 6-7 each). **(B)** Graphs show spleen weights (n= 11WT, 8KO) and absolute numbers of T cells (n= 5WT, 4KO) from aged (12 - 18 month old) mice. Data are representative from at least four independent experiments. **(C)** Representative images of immunohistochemistry staining of kidneys from WT and *Srsf1*-cKO (12 month old) mice. Original magnification, x4 (upper); x20 (lower). **(D)** Confocal imaging analysis of frozen spleen sections from wild type or *Srsf1*-cKO mice stained with fluorescent-conjugated anti-IgD, B220, CD4 and PNA-biotin followed by an Alexa 350–conjugated secondary streptavidin as described in the Methods. Original magnification, ×20. Graph shows the frequency of follicles with GCs (n=4 each). **(E)** Plots show GL-7 and Fas staining for germinal center (GC) B cells gated on live CD19+ B cells. Graph shows percent GL-7+ Fas+ B cells among live B cells (4-12wks, n= 6-7 each). **(F)** Splenocytes were stained for B220 and IgD. Plots show B220 and IgD staining gated on live B cells. Graph shows percent IgD- B cells among live B cells (n=3 each). (unpaired t-test, *p<0.05, **p<0.005)

Supplemental Figure 3.



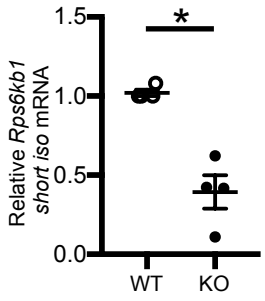
Supplemental Figure 3. Non-T cell populations in WT and *Srsf1*-cKO mice. Spleen cells were isolated from WT and *Srsf1*-cKO mice and analyzed by flow cytometry. **(A)** Plots show CD19+ B cells, CD11b+ cells and CD11c+ cells. **(B)** Graph shows percent (upper panels) and absolute numbers (lower panels) of these cells (n=18-20).

Supplemental Figure 4.



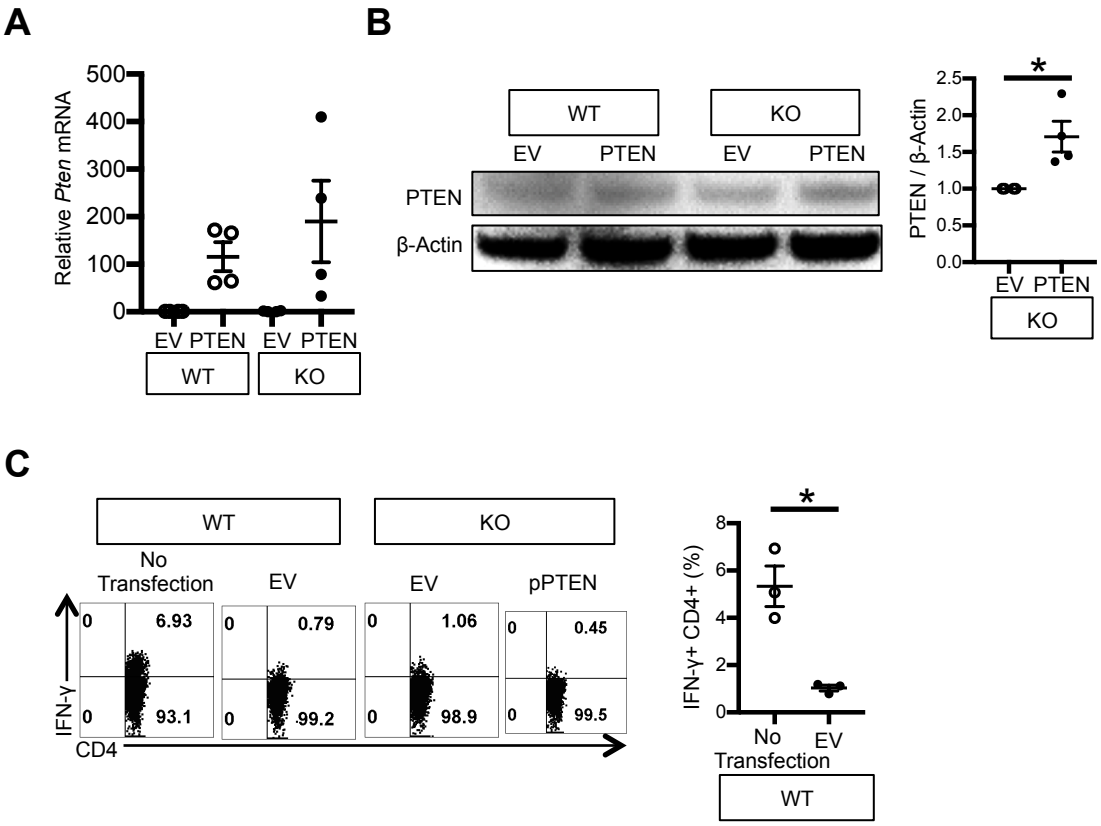
Supplemental Figure 4. Examination of Treg cells from *Srsf1*-cKO mice. (A) Spleen cells from wild-type or *Srsf1*-cKO young (6-20 weeks) and aged (12-18 months) mice were surface stained for CD4 and CD25, and intracellular stained for FoxP3 and analyzed by flow cytometry **(B)** Graphs show Treg cell frequencies (n=young 8WT, 9KO, aged 16WT, 12KO). **(C)** Conventional CD4 T (Tconv) cells were labeled with CFSE and co-cultured with Treg cells at increasing ratios for 3 days and proliferation of Tconv analyzed by flow cytometry. Representative plots are shown. **(D)** Graph shows proliferation of Tconv cells from four independent experiments (n= 4WT, 5KO).

Supplemental Figure 5.



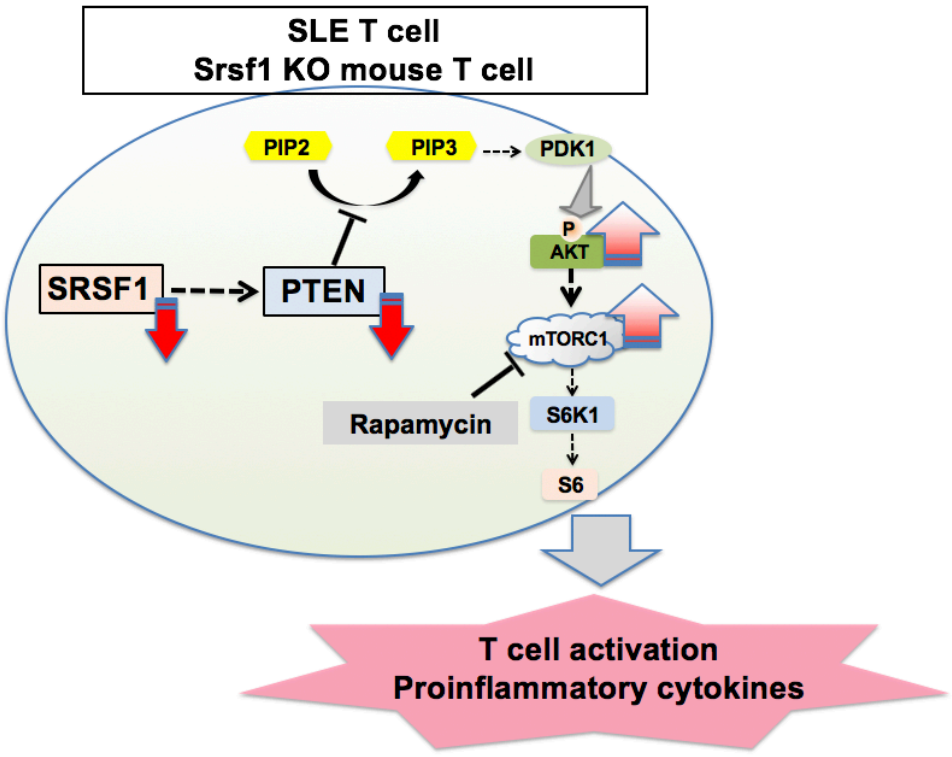
Supplemental Figure 5. Short isoform of S6K1 is decreased in T cells from *Srsf1*-cKO mice. Naïve CD4 T cells were isolated from spleen of WT and *Srsf1*-cKO mice, and stimulated with anti-CD3 (0.5 μg/ml) and CD28 (1.0 μg/ml) for 3 days. Total RNA was isolated and reverse transcribed. S6K1 (*Rps6kb1*) short isoform expression was measured by real time qPCR and normalized to housekeeping gene *cyclophilin A* (n=4 each). (unpaired t-test, *p<0.05)

Supplemental Figure 6.



Supplemental Figure 6. PTEN overexpression by transfection in mouse T cells. **(A-C)** T cells were isolated from spleens of WT or *Srsf1*-cKO mice and transfected by electroporation with empty vector (EV) or PTEN overexpression plasmid (pPTEN) or left untransfected. Sixteen hours later, cells were collected, and Pten mRNA expression levels were assessed by qPCR **(A)** and protein levels by Western blotting **(B)** (n=4 each)**. (C)** After 16h culture, cells were stimulated with PMA plus ionomycin in the presence of Monensin for 4h. Cells were collected, surface stained, fixed and permeabilized for intracellular cytokine staining. Graph shows IFN-γ-producing CD4+ cells in WT T cells without transfection and with EV transfection (n=3 each) (two-tailed paired t-test, *p<0.05).

Supplemental Figure 7.



Supplemental Figure 7. Schematic summary of the role of SRSF1 in T cells from *Srsf1*-cKO mice and SLE patients. SRSF1 contributes to the control of activation of the mTOR pathway via the regulation of PTEN expression. In T cells from KO mice and SLE patients, reduced SRSF1 levels contribute to reduced PTEN levels and increased activity of the mTOR pathway. Rapamycin blocks the mTORC1 pathway and reduces proinflammatory cytokines.

Supplemental Table 1. Demographics and clinical characteristics of SLE patients.

Table shows demographic and clinical features of SLE patients. Values shown are mean ± SD (minimum - maximum).

SLEDAI: systemic lupus erythematosus disease activity index, WBC: white blood cells

SLE Patients **Demographic and Clinical parameters**	**Values**
Number	39
Gender	Female (37), Male (2)
Race	White (16), Black (14), Asian (9)
Age (years)	34.6 ± 10.9 (20-61)
SLEDAI	2.5 ± 2.9 (0-11)
C3 (mg/dL)	106.6 ± 36.8
C4 (mg/dL)	19.5 ± 12.0
WBC (/μL)	5370 ± 2660
Lymphocytes (/μL)	1490 ± 910
Hemoglobin (gm/dL)	12.1 ± 1.5
Platelets ($x10^3$/μL)	270 ± 230
Creatinine (mg/dL)	0.74 ± 0.22
Prednisone (mg/day)	5.7 ± 8.4 (0-30)

Supplemental Table 2. Table shows list of primers and gene sequences

Genes	Primer (Forward)	Primer (Reverse)
Srsf1-Flox	GGGACTAATGTGGGAAGAATG	AACCTAAACTATTGCTCCCATCTG
dLck Cre	ATGGTGCCCAAGAAGAAGAG	CAGGTGCTGTTGGATGGTCT
PTEN	CATTGCCTGTGTGTGGTGATA	AGGTTTCCTCTGGTCCTGGTA
S6K1 (short-iso)	GAGGAGAACTATTTATGCAGTTAG	GGGGCACTTCATCCCTAAGG
Cyclophilin A	GGGTTCCTCCTTTCACAGAA	GATGCCAGGACCTGTATGCT