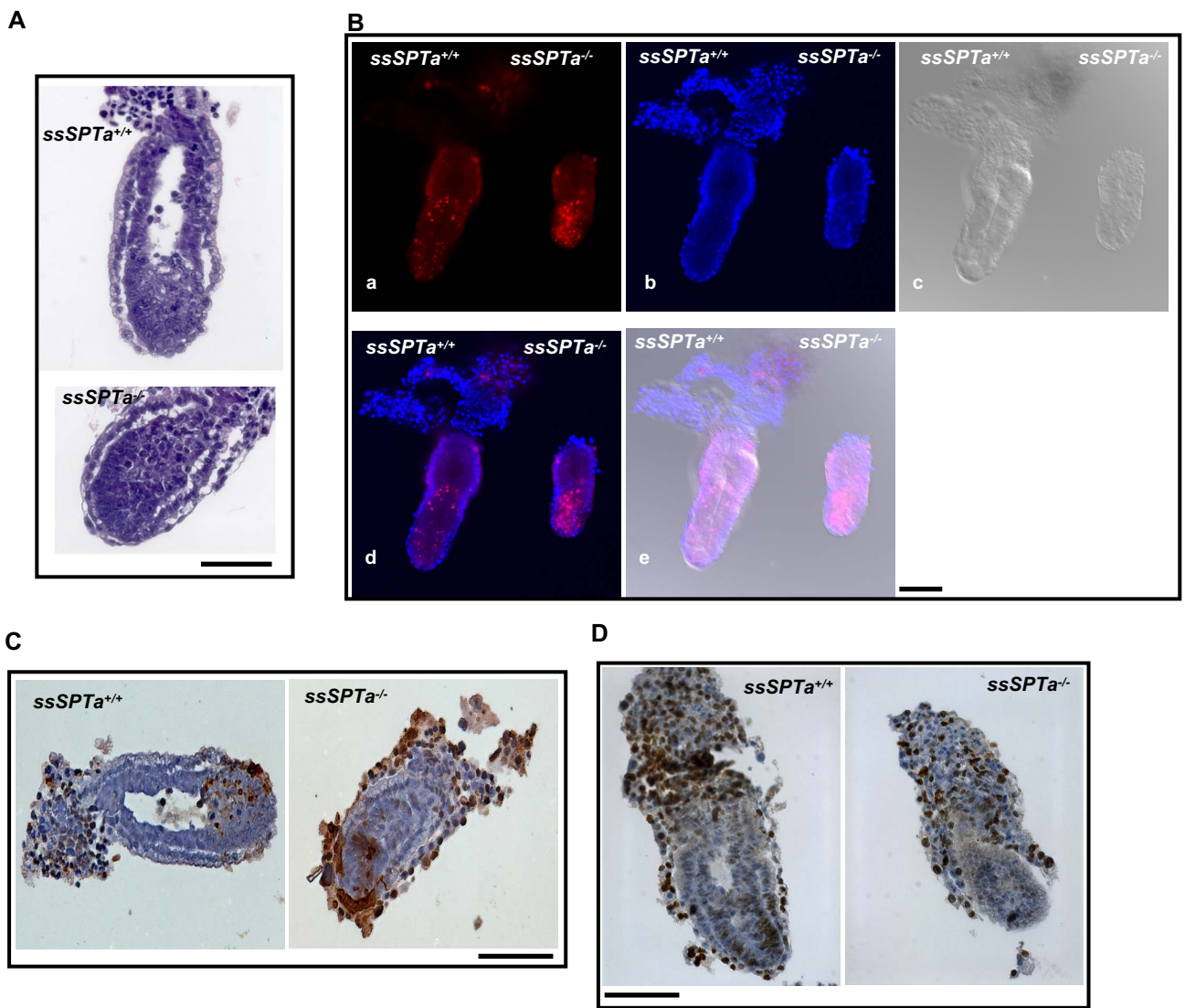
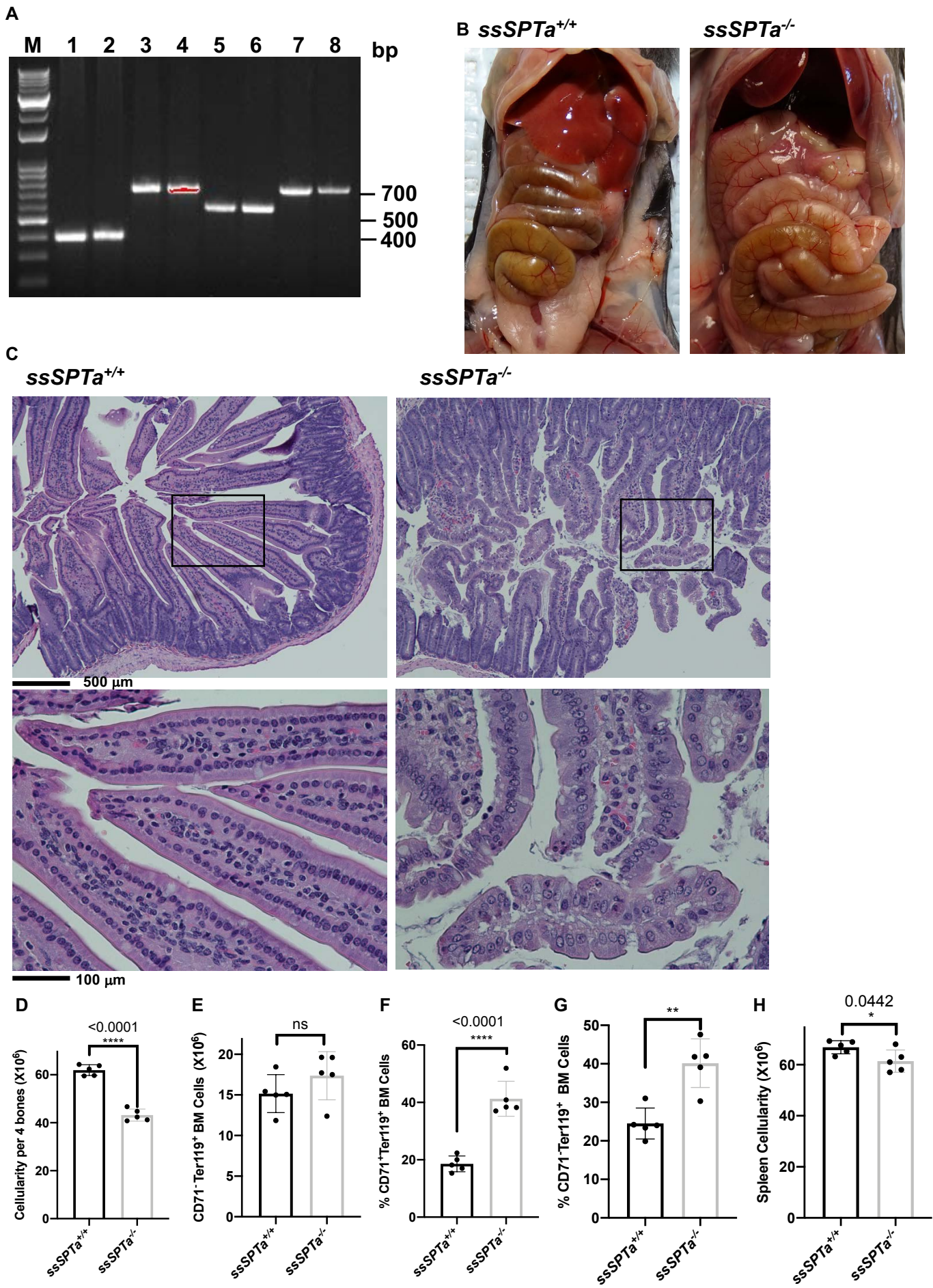


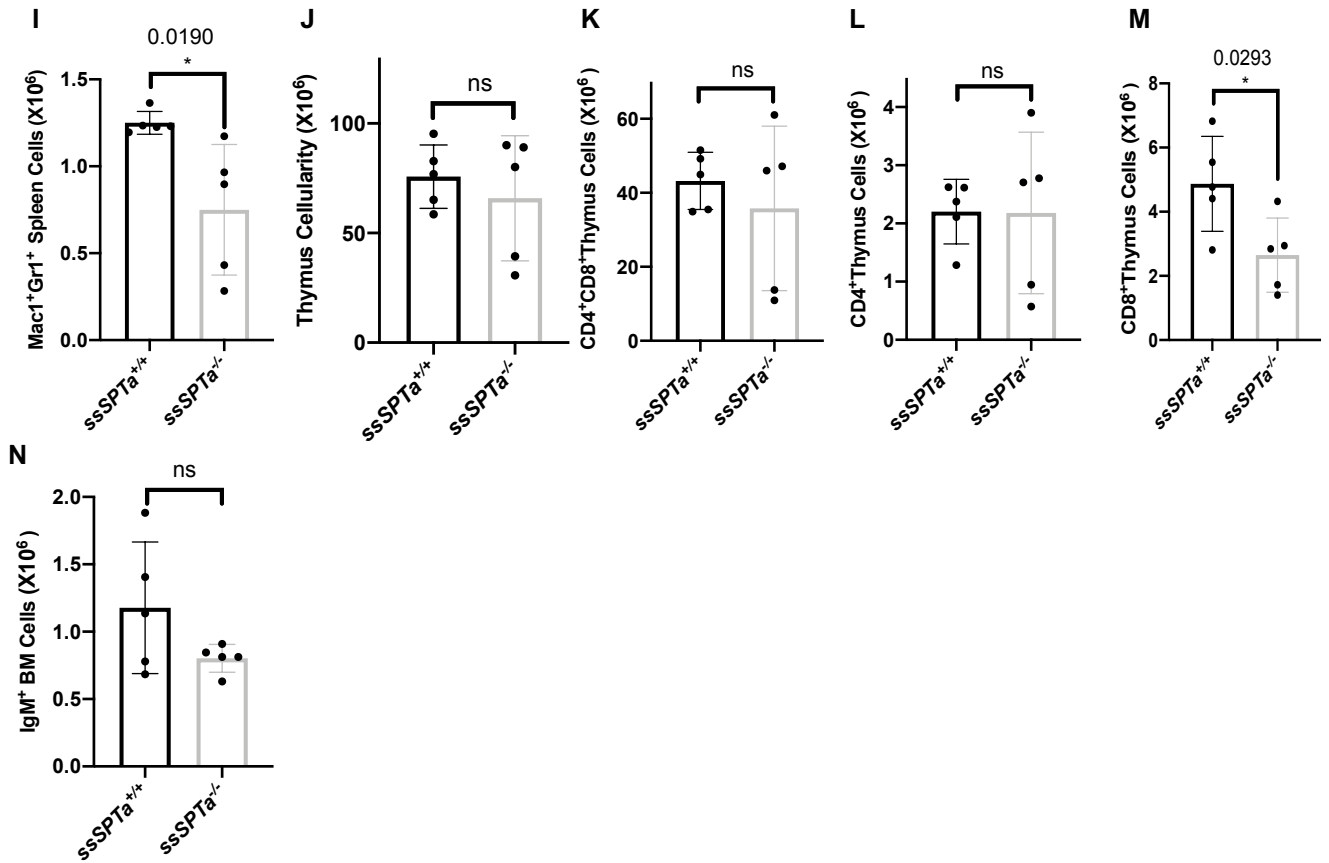
<b>Category</b>	<b>Total no.</b>	<b><i>ssSPTa</i><sup>+/+</sup></b>	<b><i>ssSPTa</i><sup>+/-</sup></b>	<b><i>ssSPTa</i><sup>-/-</sup></b>	<b>No. absorbed</b>	<b>ND</b>
<b>Live births</b>	<b>289</b>	<b>105</b>	<b>184</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>Blastocyst (E3.5)</b>	<b>10</b>	<b>3</b>	<b>5</b>	<b>2</b>	<b>-</b>	<b>-</b>
<b>Embryos (E6.5)</b>	<b>24</b>	<b>3</b>	<b>12</b>	<b>4</b>	<b>3</b>	<b>2</b>
<b>Embryos (E7.5)</b>	<b>62</b>	<b>18</b>	<b>33</b>	<b>1</b>	<b>8</b>	<b>2</b>
<b>Embryos (E8.5)</b>	<b>20</b>	<b>5</b>	<b>12</b>	<b>0</b>	<b>3</b>	<b>-</b>

**Supplemental Table1.** Matings were set between *ssSPTa*<sup>+/-</sup>. Blastocyst and embryos were harvested at E3.5, E6.5, E7.5 and E8.5 to ascertain the time of embryonic lethality of *ssSPTa*<sup>-/-</sup>. The table lists the genotypes obtained from *ssSPTa* heterozygous crosses.

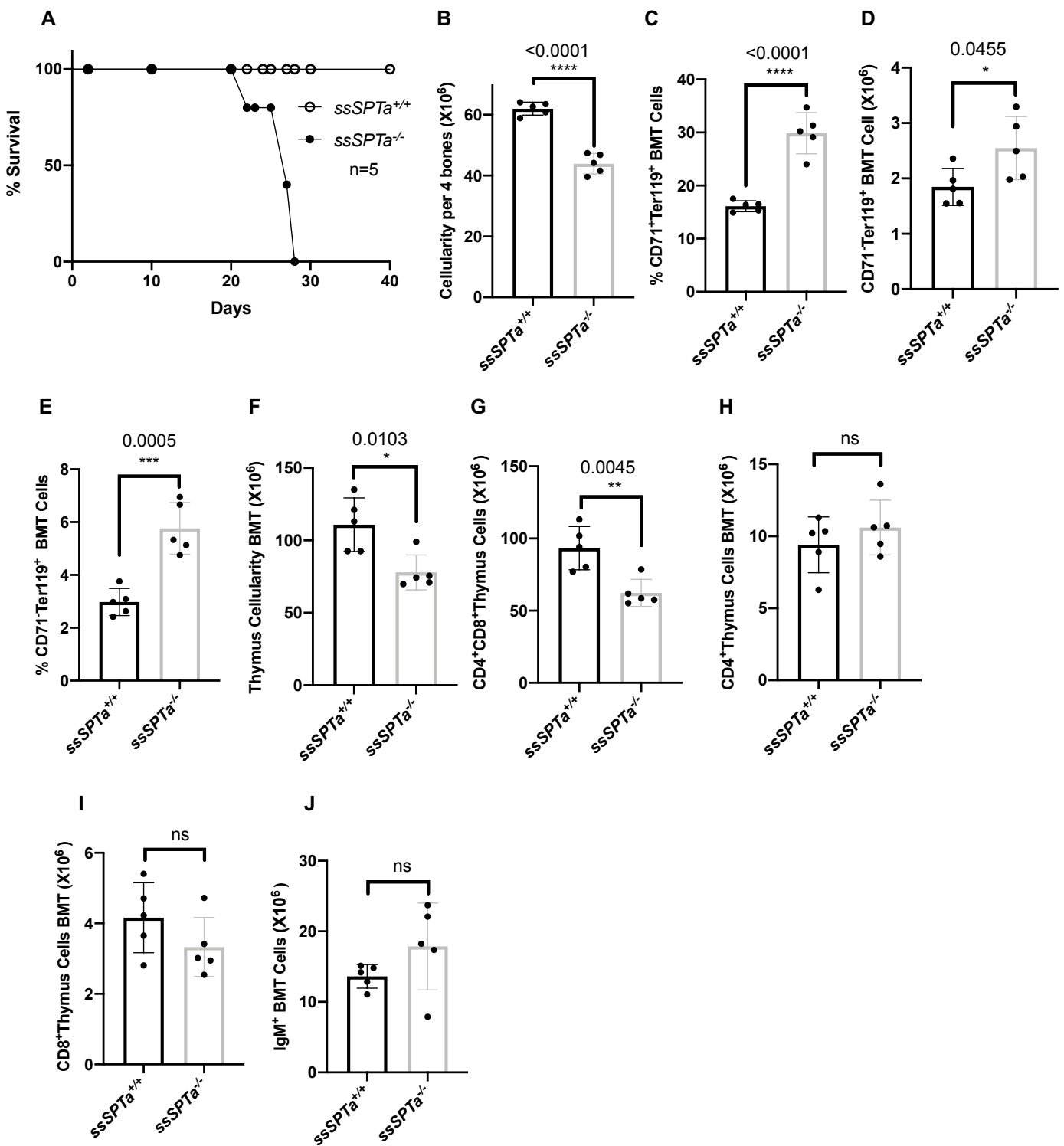


**Figure S1.** *ssSPTa* deletion cause embryonic lethality at E6.5. **A.** *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> embryos harvested at E6.5 stained with hematoxylin and eosin. **B.** *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> embryos were harvested at E6.5 and stained for **a** lysotracker; red **b** DAPI; blue, **c** DIC, **d** merge of lyso tracker and DAPI, **e** merge of lyso tracker, DAPI and DIC. **C.** *ssSPTa*<sup>-/-</sup> embryos at E6.5 showed more TUNEL positive cells indicative of apoptosis than control. **D.** *ssSPTa*<sup>-/-</sup> embryos at E6.5 showed less uptake of BrdU than control indicative of reduced cell proliferation. All graphs are represented as mean  $\pm$  SEM. P value <0.05 is significant, calculated from unpaired t-test. **Scale bar 100  $\mu$ m.**



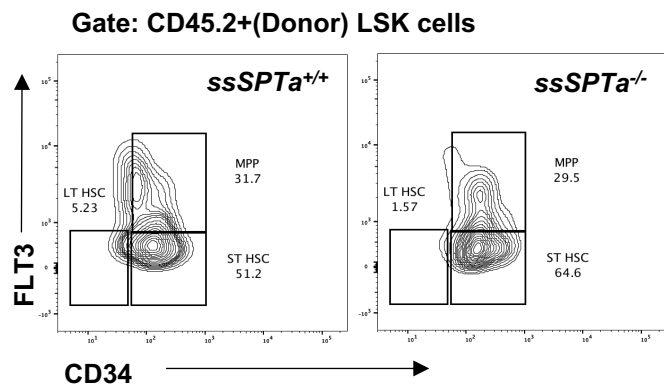


**Figure S2.** Deletion of *ssSPTa* using *Mx1-Cre* compromises hematopoiesis. **A.** PCR based genotyping of *ssSPTa* wildtype and its floxed allele. Flox allele PCR for *ssSPTa<sup>flox/flox</sup>:Mx-1 Cre* (1 & 2, Flox band) mice. *Cre* allele PCR for *ssSPTa<sup>flox/flox</sup>:Mx-1 Cre* (3 & 4, Cre band) mice. Wild type allele PCR for *ssSPTa<sup>+/+</sup>:Mx-1 Cre* (5 & 6, Wild type band) mice. *Cre* allele PCR for *ssSPTa<sup>+/+</sup>:Mx-1 Cre* (7 & 8, Cre band) mice. The flox, wild type and Cre PCR amplicons appear at 397, 575 and 700bp, respectively. **B.** Photograph of *ssSPTa<sup>+/+</sup>* and *ssSPTa<sup>-/-</sup>* mice four days after poly(I:C) injection showing fluid accumulation in the mutant small intestine. **C.** H&E-staining of small intestine from *ssSPTa<sup>+/+</sup>* and *ssSPTa<sup>-/-</sup>* mice visualized at 10X (scale bar 500  $\mu$ m) and rectangular marquee area magnified to 40X (scale bar 100  $\mu$ m). **D.** BM cellularity from two femurs and two tibia on day eight in the *ssSPTa<sup>+/+</sup>* and *ssSPTa<sup>-/-</sup>* mice (n = 5). **E.** The total numbers of CD71<sup>+</sup>Ter119<sup>+</sup> cells, **F.** The percent of CD71<sup>+</sup>Ter119<sup>+</sup> BMCs, **G.** The percent of CD71<sup>+</sup>Ter119<sup>+</sup> BMCs were plotted for the *ssSPTa<sup>+/+</sup>* and *ssSPTa<sup>-/-</sup>* mice (n = 5). **H.** Spleen cellularity was determined on day eight in the *ssSPTa<sup>+/+</sup>* and *ssSPTa<sup>-/-</sup>* mice (n = 5). **I.** The total numbers of spleen Mac1<sup>+</sup>Gr1<sup>+</sup> cells were plotted. **J.** Thymus cellularity was determined eight days after poly(I:C) injection. **K.** The total numbers of CD4<sup>+</sup>CD8<sup>+</sup> cells from thymus were plotted (n = 5). **L.** The total numbers of CD4<sup>+</sup> cells from the thymus were plotted (n = 5). **M.** The total numbers of CD8<sup>+</sup> cells from the thymus were (n = 5). **N.** The total numbers of IgM<sup>+</sup> BM cells were plotted. All graphs are represented as mean  $\pm$  SEM. P value <0.05 is significant, calculated from unpaired t-test.

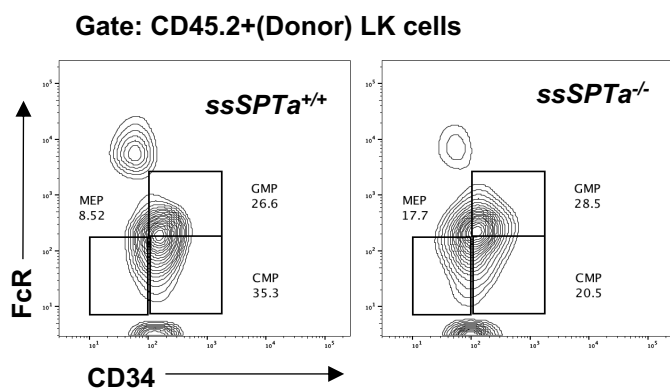


**Figure S3.** *ssSPTa* deletion impairs myeloid differentiation and spares erythroid differentiation in chimeric mice. **A.** Survival graph of *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> BMT mice after poly(I:C) injection in chimeric mice. **B.** BMT cellularity was determined for the *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> twenty-one days after poly(I:C) injection in chimeric mice (n = 5). **C.** The percent CD71<sup>+</sup>Ter119<sup>+</sup> cells were plotted for the transplanted *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> mice (n=5). **D.** The total numbers of CD71<sup>+</sup>Ter119<sup>+</sup> cells were plotted for the transplanted *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> mice (n=5). **E.** The percent CD71<sup>+</sup>Ter119<sup>+</sup> cells were plotted for the *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> mice (n=5). **F.** Thymus cellularity of BMT was determined for the *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> twenty-one days after poly(I:C) injection (n = 5). **G.** The total numbers of donor CD4<sup>+</sup>CD8<sup>+</sup> cells from thymus were plotted (n = 5). **H.** The total numbers of donor CD4<sup>+</sup> cells from the thymus were plotted (n = 5). **I.** The total numbers of donor CD8<sup>+</sup> cells from the thymus were plotted (n = 5). **J.** The total numbers of IgM<sup>+</sup> BMT cells were plotted. All graphs are represented as mean ± SEM. P value < 0.05 is significant, calculated from unpaired t-test.

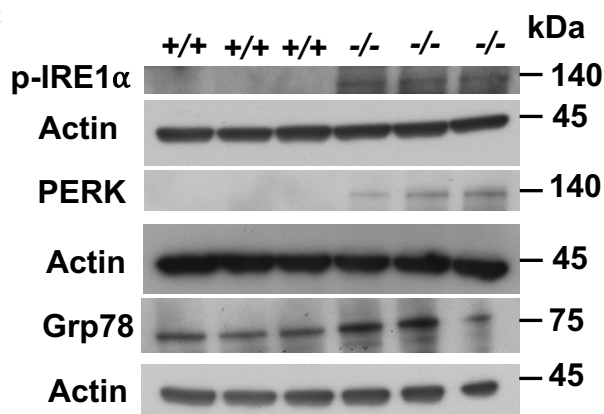
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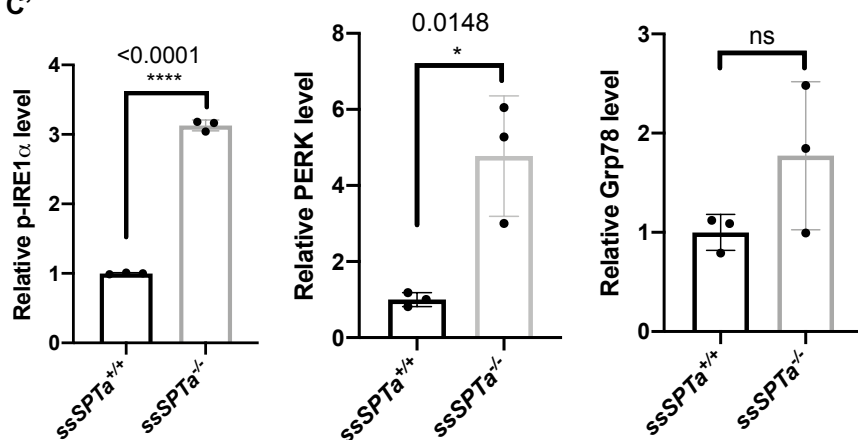
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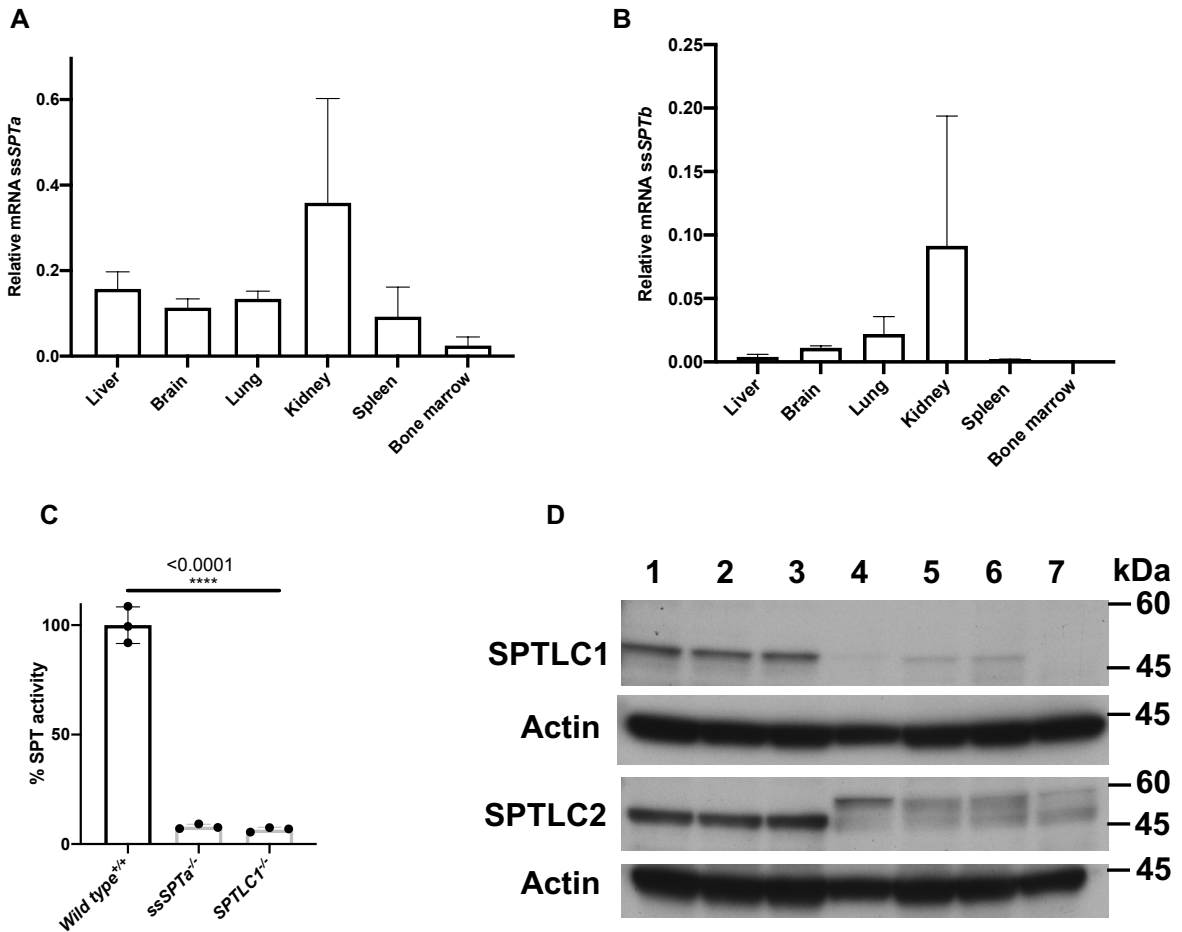
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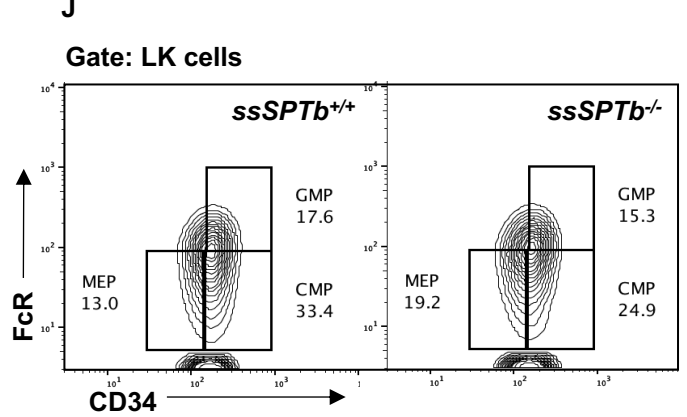
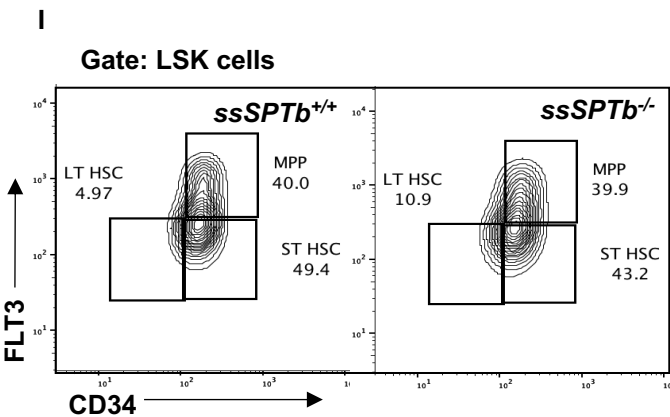
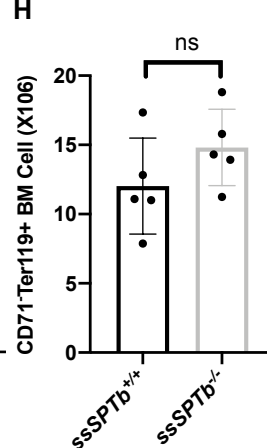
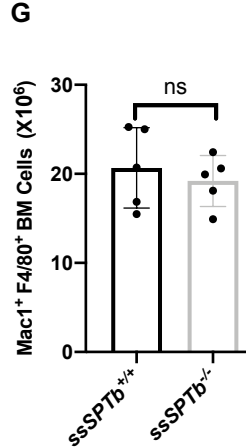
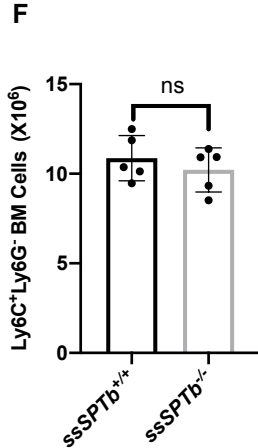
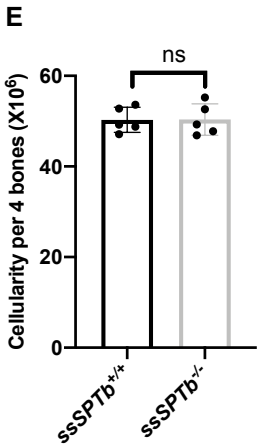
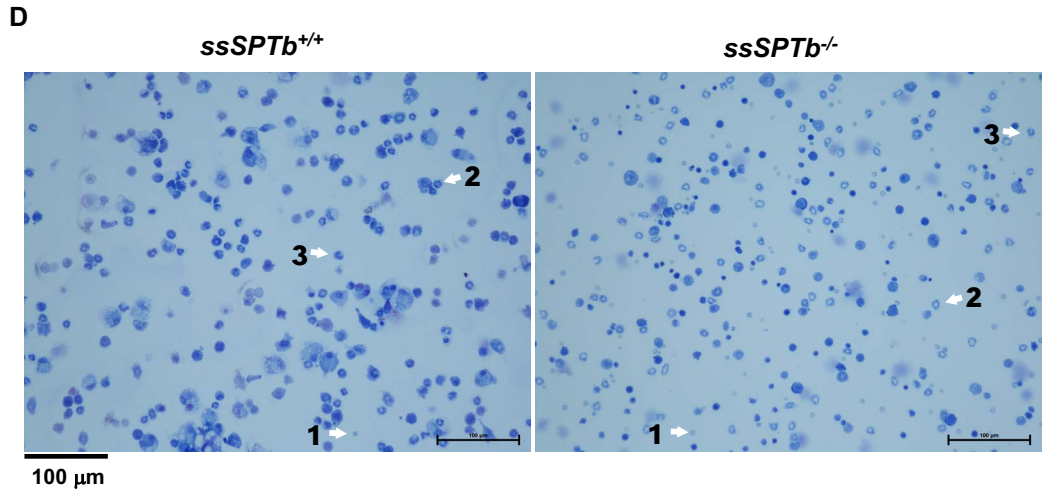
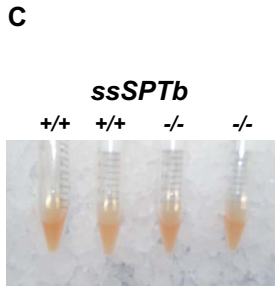
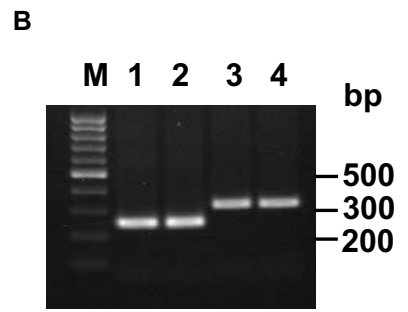
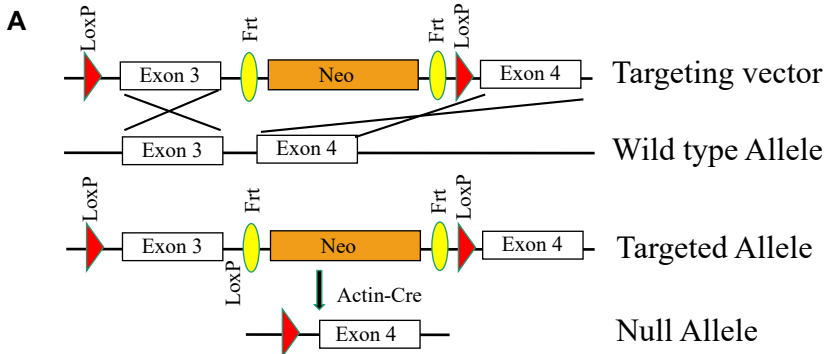
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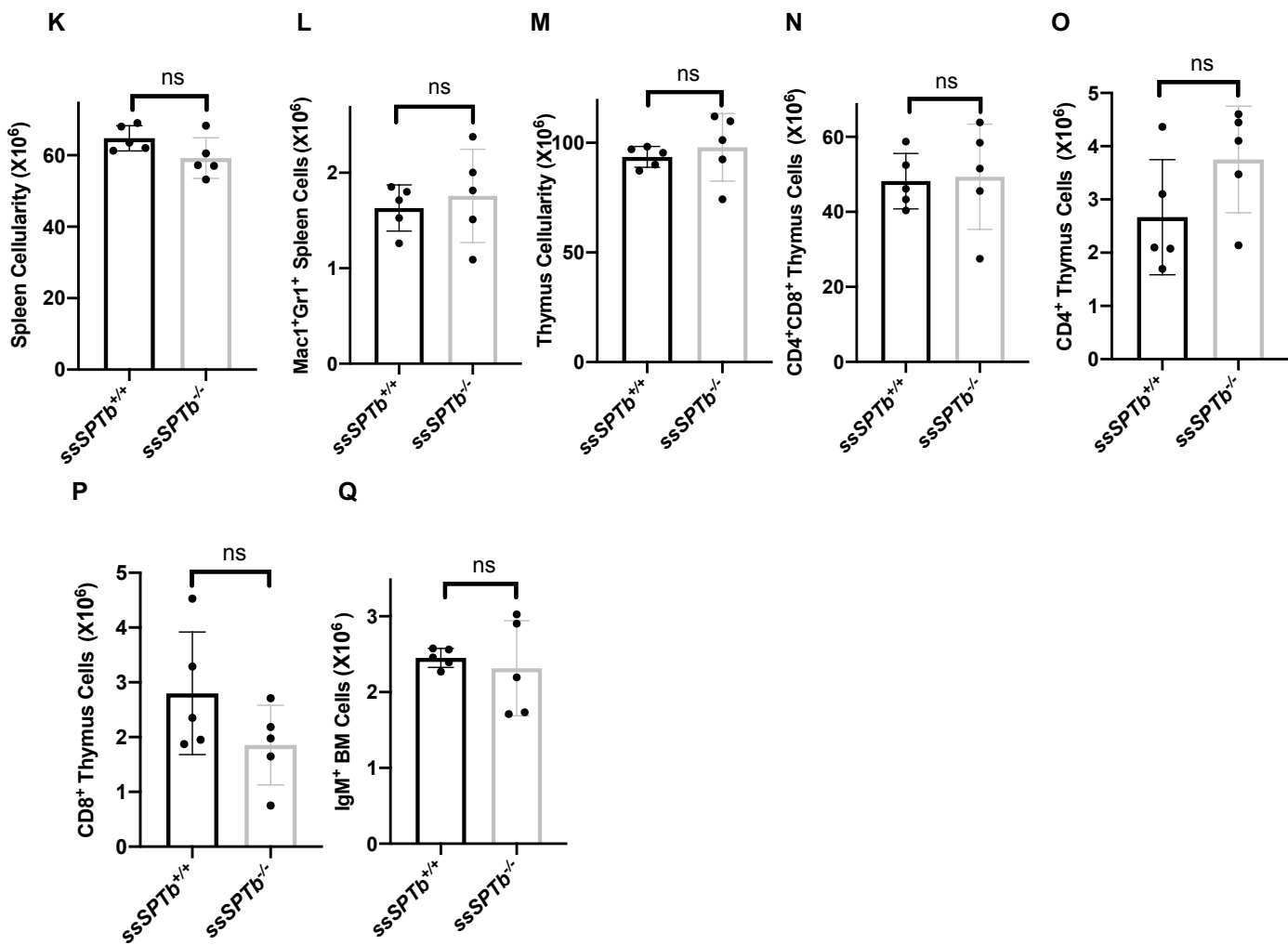
**Figure S4.** Stem cell analysis of transplanted bone marrow cells and western blot of bone marrow cells. **A.** The LSK population was sub-gated for LT-HSCs, ST-HSCs and MPPs by Flt3 and CD34 staining for the *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> mice. **B.** The LK population was sub-gated for CMPs, GMPs and MEPs by FcR and CD34 staining for the *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> mice. **C.** Western blot analysis of bone marrow cell extracts of *ssSPTa*<sup>+/+</sup> and *ssSPTa*<sup>-/-</sup> mice four days after poly(I:C) injection probed for p-IRE1α, PERK and Grp78. **C'.** Quantitative data representative of three independent experiments. All graphs are represented as mean ± SEM. P value <0.05 is significant, calculated from unpaired t-test.



**Figure S5.** SPT complex stability and activity. **A.** Real time qPCR analysis of *ssSPTa* mRNA expression in liver, brain, lung, kidney, spleen and bone marrow isolated from wild type mice. Gene expression was normalized to  $\beta$ -actin. qPCR results were from three independent experiments. **B.** Real time qPCR analysis of *ssSPTb* mRNA expression in liver, brain, lung, kidney, spleen and bone marrow isolated from wild type mice. Gene expression was normalized to  $\beta$ -actin. qPCR results were from three independent experiments (n = 3). **C.** The percentage of SPT activity from liver microsomes preparation from wild type, *ssSPTa*<sup>-/-</sup> and *SPTLC1*<sup>-/-</sup>. The results were from three independent experiments. **D.** Western blot analysis of bone marrow cell extracts of *ssSPTa*<sup>+/+</sup>(1,2,3), *ssSPTa*<sup>-/-</sup>(4,5,6) and *SPTLC1*<sup>-/-</sup> (7) mice four days after poly(I:C) injection probed with SPTLC1 and SPTLC2 antibodies. All graphs are represented as mean  $\pm$  SEM. P value <0.05 is significant, calculated from unpaired t-test.







**Figure S6.** Deletion of *ssSPTb* does not compromise hematopoiesis. PCR based genotyping of *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup>. **A.** Deletion of exon 3 knocks the *ssSPTb* gene out. **B.** PCR for *ssSPTb*<sup>+/+</sup> (1&2) and *ssSPTb*<sup>-/-</sup> (3&4) alleles. The Control and *ssSPTb* mutant PCR amplicons appear at 250 and 350bp, respectively. **C.** Bone marrow tissue isolated from *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice. **D.** Wright-Giemsa staining of BMCs from the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice. 1 - RBC, and 2-metamyelocyte, and 3-segmented band cell. **E.** BM cellularity from two femurs and two tibia in the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice (n = 5). **F.** Ly6C<sup>+</sup>Ly6G<sup>-</sup>, **G.** Mac-1<sup>+</sup>F4/80<sup>+</sup> cells were plotted for the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice (n = 5). **H.** CD71-Ter119<sup>+</sup> cells, were plotted for the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice (n = 5). **I.** The LSK population was sub-gated for LT-HSCs, ST-HSCs and MPPs by Flt3 and CD34 staining for the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice. **J.** The LK population was sub-gated for CMPs, GMPs and MEPs by FcR and CD34 staining for the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice. **K.** Spleen cellularity was determined in the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice (n = 5). **L.** The total numbers of spleen Mac1<sup>+</sup>Gr1<sup>+</sup> cells were plotted. **M.** Thymus cellularity was determined in the *ssSPTb*<sup>+/+</sup> and *ssSPTb*<sup>-/-</sup> mice (n = 5). **N.** The total numbers of CD4<sup>+</sup>CD8<sup>+</sup> cells from thymus were plotted (n = 5). **O.** The total numbers of CD4<sup>+</sup> cells from the thymus were plotted (n = 5). **P.** The total numbers of CD8<sup>+</sup> cells from the thymus were plotted (n = 5). **Q.** The total numbers of IgM<sup>+</sup> BMCs were plotted (n = 5). All graphs are represented as mean  $\pm$  SEM. P value <0.05 is significant, calculated from unpaired t-test.