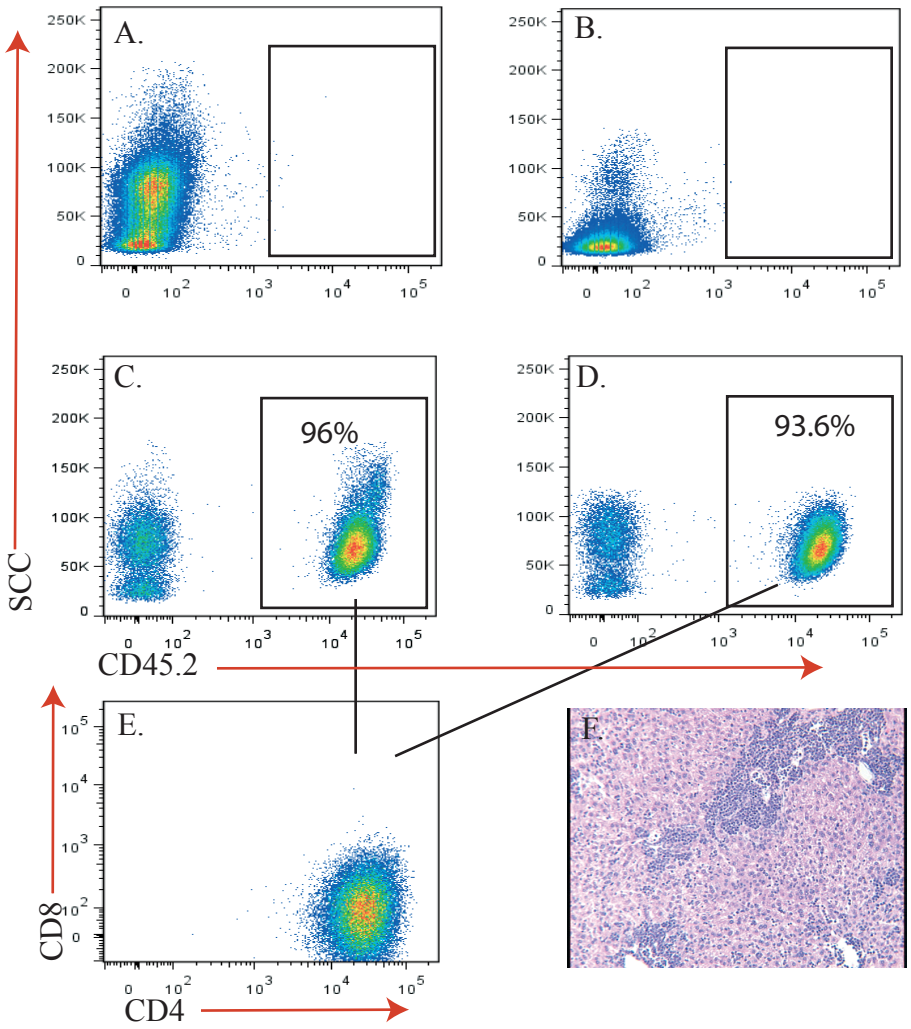
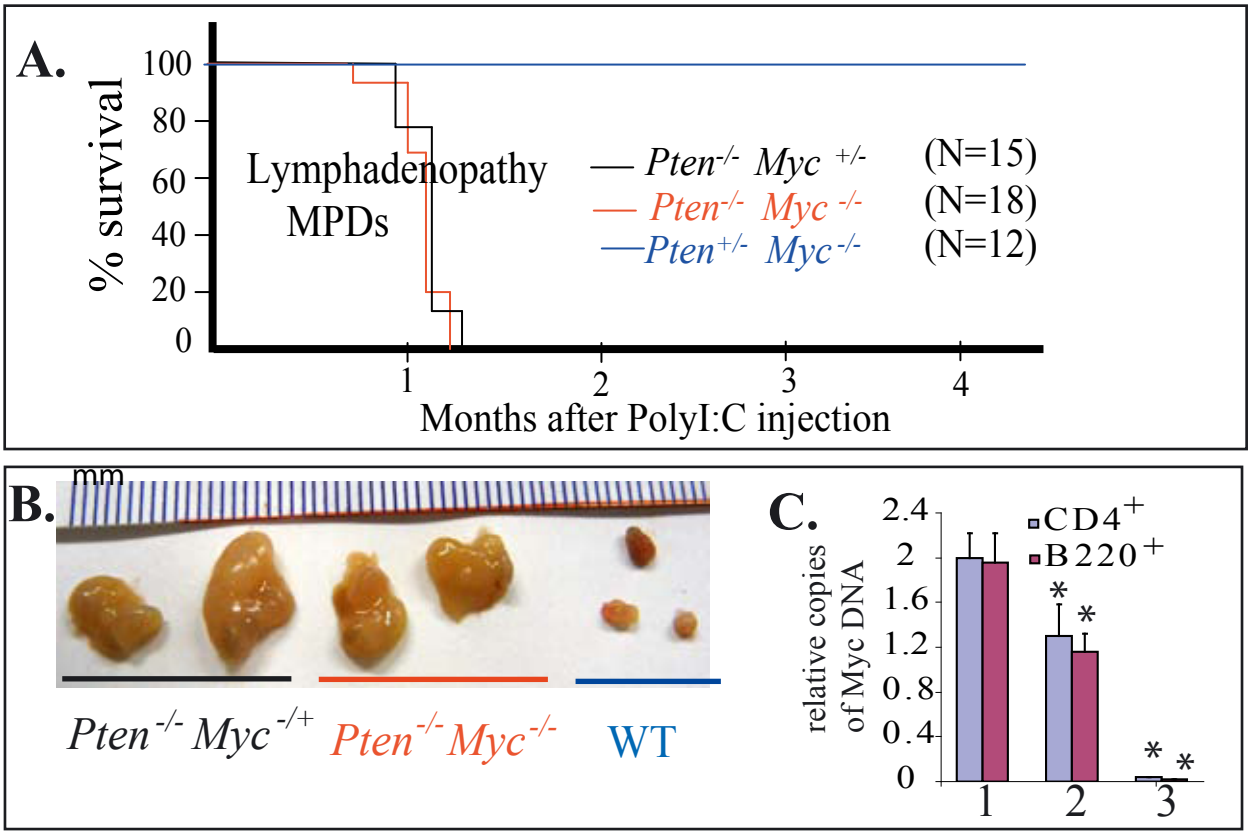
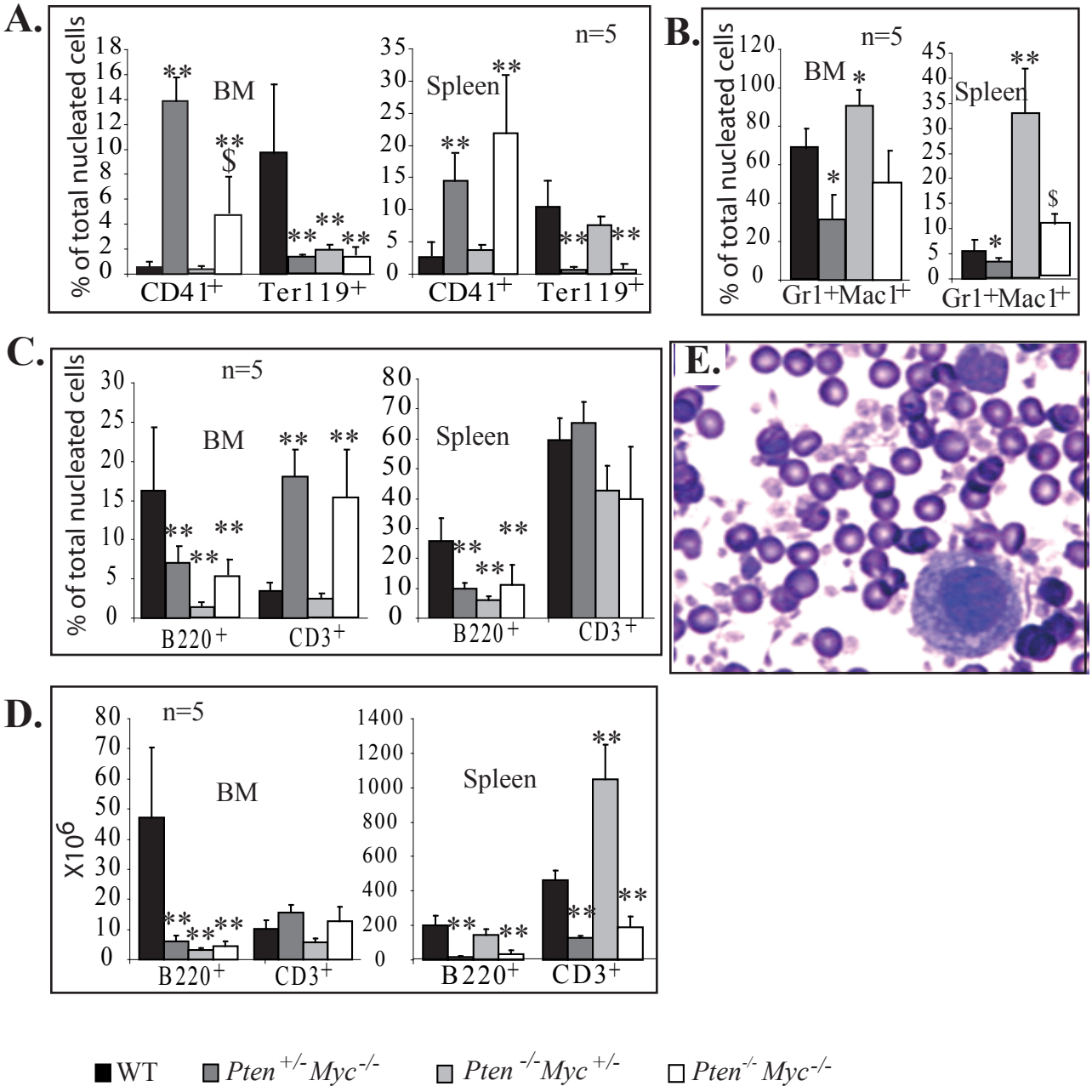


Supplementary Data 1. ***Lymphocytes isolated from Cre^{+}Pten$^{fx/fx}$/Myc$^{fx/fx}$ LPDs mice failed to engraft to hematopoietic tissues in recipient mice, whereas lymphoblasts from Cre^{+}Pten$^{fx/fx}$/Myc$^{fx/+}$ mice with lymphoma generated a leukemia-like disease with lymphoblast infiltration into multiple tissues.*** Lymphocytes and lymphoblasts were isolated from the enlarged lymph nodes of *Cre^{+}Pten$^{fx/fx}$/Myc$^{fx/fx}$* mice with LPDs and *Cre^{+}Pten$^{fx/fx}$Myc$^{fx/+}$* mice with lymphoma. Cells were transplanted into lethally- irradiated recipient mice separately. Ten million *Cre^{+}Pten$^{fx/fx}$/Myc$^{fx/fx}$* LPD lymphocytes (CD45.2^{+}) or one million *Cre^{+}Pten$^{fx/fx}$/Myc$^{fx/+}$* lymphoblasts (CD45.2^{+}) were transplanted into each recipient mouse together with 2×10^{5} WT supporting BM cells (CD45.1^{+}). Eight mice were transplanted in each group. Mice receiving *Cre^{+}Pten$^{fx/fx}$/Myc$^{fx/fx}$* LPD lymphocytes survived for more than 6 months. No donor- derived cells (CD45.2^{+}) could be detected in BM (**A**) and spleens (**B**) of recipient mice 6 months after transplantation, as shown by flow cytometric analysis of CD45.2^{+} cells. However, all mice receiving *Cre^{+}Pten$^{fx/fx/}$Myc$^{fx/+}$* lymphoblasts died within 20 days after transplantation with a leukemia-like disease as shown by multiple tissue infiltration of CD4^{+}CD8^{-} lymphoblasts (**C-F**). **C** and **D** are representative flow data from BM (**C**) and spleen (**D**) of one such recipient mouse. **F**. A representative liver section shows lymphoblast infiltration of the liver tissue.

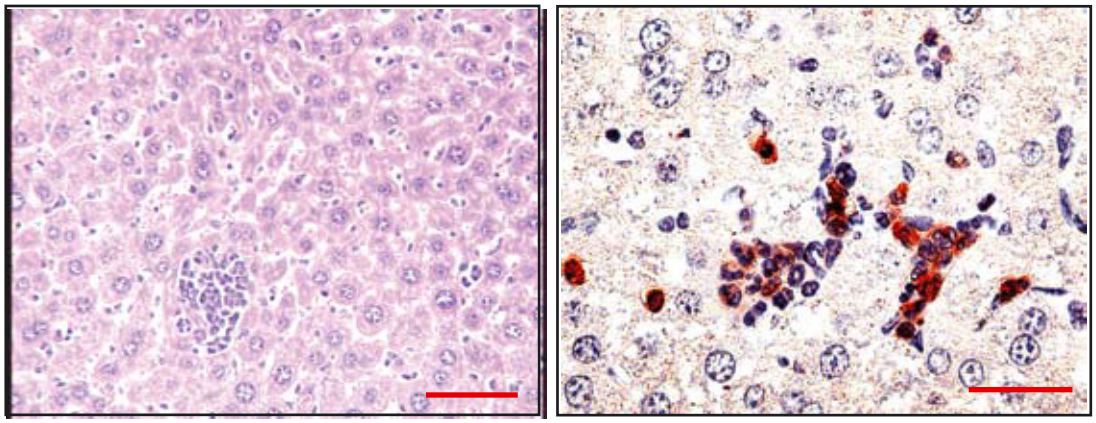


Supplementary Data 2. **A & B.** Three weeks after birth, *Mx1Cre*$^{+}$*Pten*$^{fx/fx}$*Myc*$^{fx/fx}$, *Mx1Cre*$^{+}$*Pten*$^{fx/fx}$*Myc*$^{fx/+}$, *Mx1Cre*$^{+}$*Pten*$^{fx/+}$*Myc*$^{fx/fx}$, and WT littermate control mice were injected with 200ug. polyI:C every other day for a total of 5 injections to induce gene deletions. All *Mx1Cre*$^{+}$*Pten*$^{fx/fx}$*Myc*$^{fx/fx}$ and *Mx1Cre*$^{+}$*Pten*$^{fx/fx}$*Myc*$^{fx/+}$ mice developed lymphadenopathy 20 to 30 days after *Pten* and *Myc* gene deletions were induced. **C.** Heterozygous or homozygous *Myc* deletion in CD4^{+} and B220^{+} lymphocytes isolated from enlarged lymph nodes were confirmed by q-PCR assay. 1, 2 and 3 represent CD4^{+} or B220^{+} cells isolated from WT lymph nodes, *Mx1Cre*$^{+}$*Pten*$^{fx/fx}$*Myc*$^{fx/+}$ lymphadenopathy and *Mx1Cre*$^{+}$*Pten*$^{fx/fx}$*Myc*$^{fx/fx}$ lymphadenopathic,mice, respectively

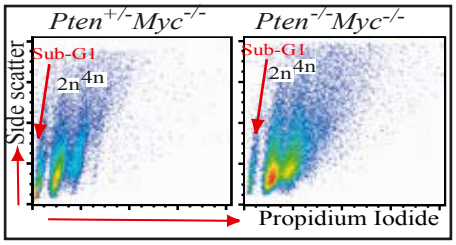


Supplementary Data 3: General hematopoietic information for *Pten*$^{-/-}$*Myc*$^{-/-}$ mice. **A.** Reduction in the percentage of CD41^{+} megakaryocytes in BM but increased percentage of these same cells in spleens of *Pten*$^{-/-}$*Myc*$^{-/-}$ mice compared to *Pten*$^{+/-}$*Myc*$^{-/-}$ mice. **B.** Slight increase in the percentage of Gr1^{+}Mac1^{+} granulocytes in spleens of *Pten*$^{-/-}$*Myc*$^{-/-}$ mice compared to those of *Pten*$^{+/-}$*Myc*$^{-/-}$ mice. **C.** Significant reduction in B220^{+} B lymphocytes in BM and spleens of *Pten*$^{-/-}$*Myc*$^{-/-}$ and *Pten*$^{+/-}$*Myc*$^{-/-}$ mice. However the percentage of CD3^{+} T-lymphocytes is significantly increased in BM but remains the same in spleens of *Pten*$^{-/-}$*Myc*$^{-/-}$ and *Pten*$^{+/-}$*Myc*$^{-/-}$ mice compared to WT control mice. The percentages of these two types of cells are comparable between *Pten*$^{-/-}$*Myc*$^{-/-}$ and *Pten*$^{+/-}$*Myc*$^{-/-}$ mice. **D.** Absolute numbers of B220^{+} B-lymphocytes and CD3^{+} T-lymphocytes are comparable between *Pten*$^{-/-}$*Myc*$^{-/-}$ and *Pten*$^{+/-}$*Myc*$^{-/-}$ mice. **E.** A few megakaryocytes are occasionally observed in the PB of *Pten*$^{-/-}$ *Myc*$^{-/-}$ mice. ** indicates statistical significance compared to *WT* mice. $ indicates statistical significance compared to *Pten*$^{-/-}$*Myc*$^{+/-}$ mice.

Pten$^{-/-}$*Myc*$^{+/-}$

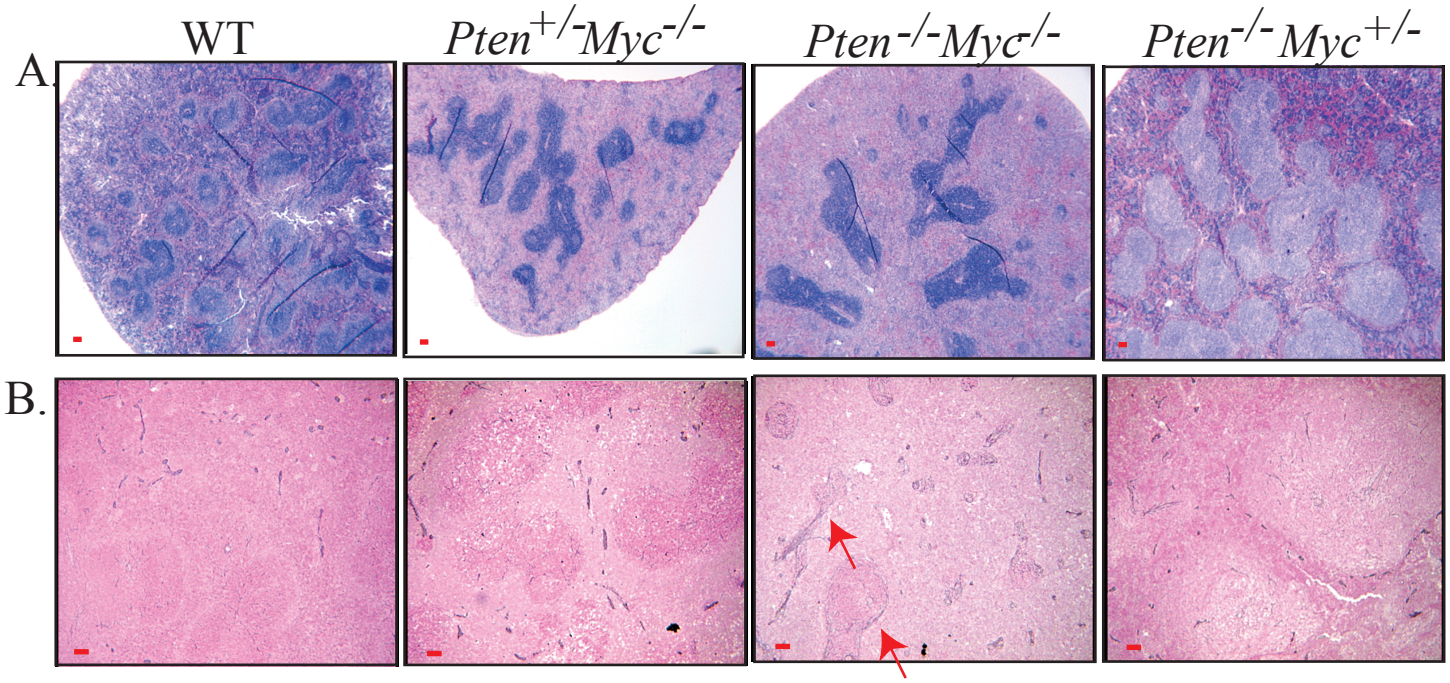


Supplementary data 4. Granulocyte infiltration into livers of *Pten*$^{-/-}$*Myc*$^{+/-}$ mice, as shown by Gr1 antibody staining. Bars in the figures equal 100 μm.

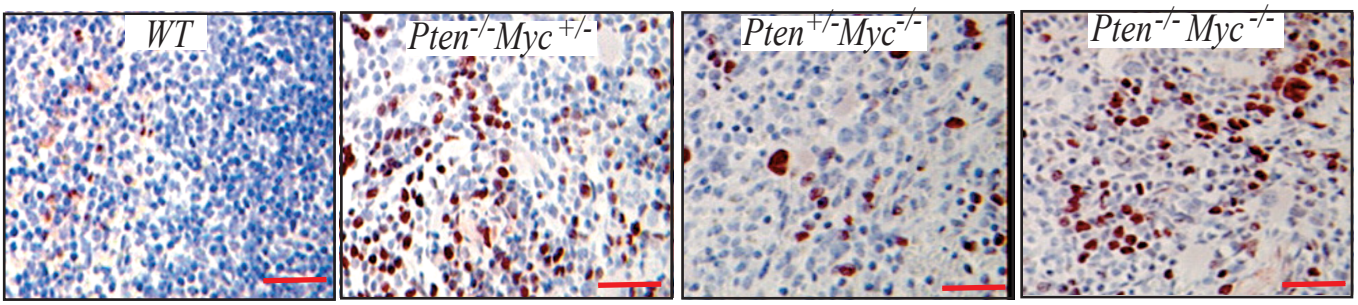


%	Sub-G1	2n	4n	8n	16n
Pten$^{+/-}$*Myc*$^{-/-}$	21.3	42.1	26.2	6.1	2.2
Pten$^{-/-}$ *Myc*$^{-/-}$	18.7	33.3	32.6	9.7	2.9

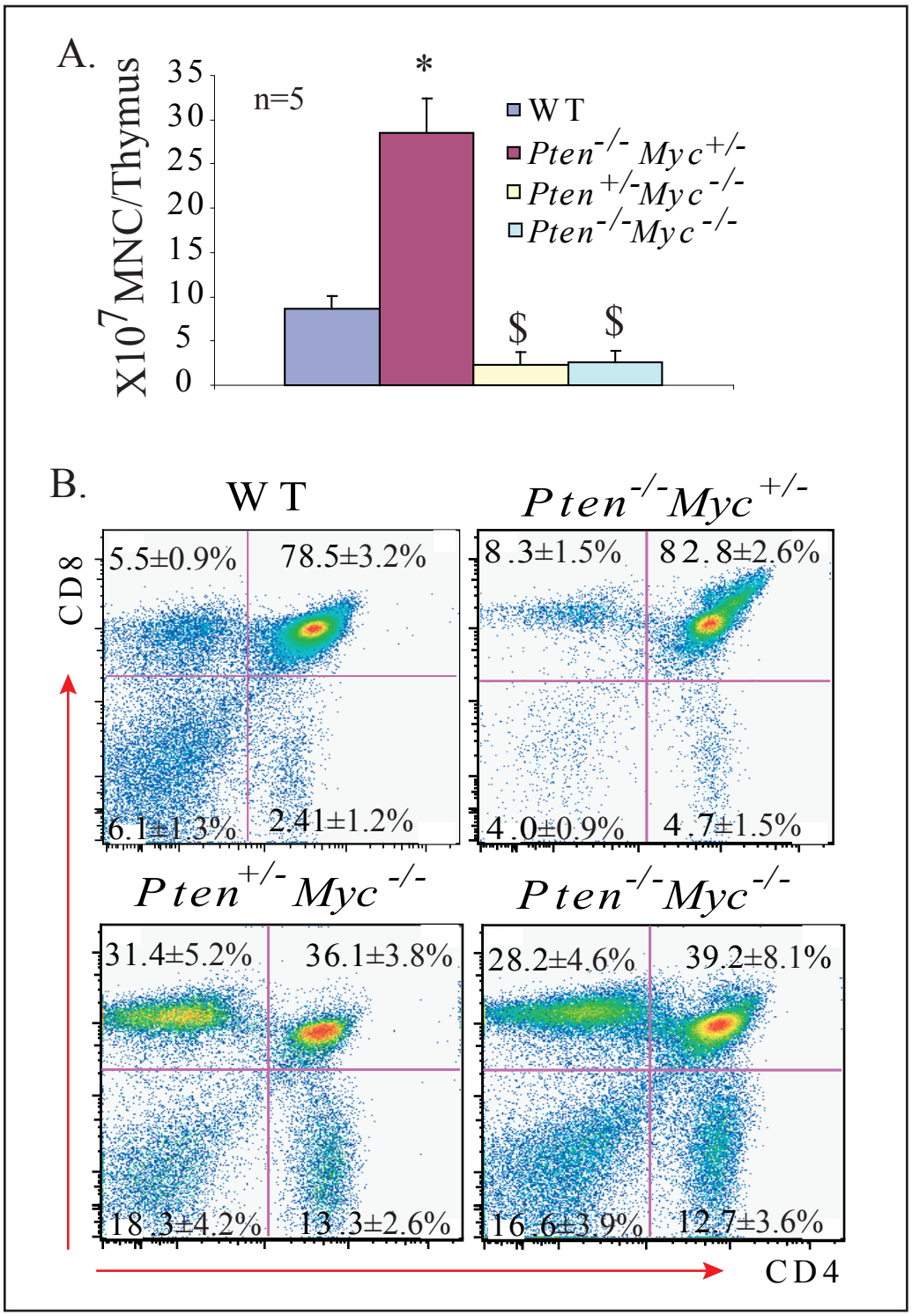
Supplementary Data 5. *Pten* deletion did not reverse the lower ploidy and increased apoptosis phenotype of *Myc*$^{-/-}$ megakaryocytes. PI staining and flow cytometric analysis of DNA content of CD41^{+} megakaryocytes from *Pten*$^{+/-}$ *Myc*$^{-/-}$ and *Pten*$^{-/-}$ *Myc*$^{-/-}$ mice. Upper panel is representative flow cytometric data for three pairs of mouse analyses. The sub-G1 population consists of cells undergoing apoptosis.



Supplementary Data 6. Increased fibrosis in the spleens of *Pten*$^{-/-}$*Myc*$^{-/-}$ mice. A & B. Spleen sections of WT, *Pten*$^{+/-}$ *Myc*$^{-/-}$, *Pten*$^{-/-}$ *Myc*$^{-/-}$ and *Pten*$^{+/-}$ *Myc*$^{-/-}$ mice stained with H & E (**A**) and reticulin (**B**). Increased fibrosis in *Pten*$^{-/-}$ *Myc*$^{-/-}$ mouse spleen is indicated by with arrows (**B**). Bars in the figures equal 100μm.



Supplementary Data 7. Increased megakaryocytic proliferation in *Pten*$^{-/-}$*Myc*$^{-/-}$ mice.
Representative images of *in situ* BrdU staining of spleen sections from WT, *Pten*$^{-/-}$*Myc*$^{+/-}$, *Pten*$^{+/-}$*Myc*$^{-/-}$ and *Pten*$^{-/-}$*Myc*$^{-/-}$mice. Significantly increased BrdU^{+} cell percentage in spleens of *Pten*$^{-/-}$*Myc*$^{+/-}$ and *Pten*$^{-/-}$ *Myc*$^{-/-}$mice. The BrdU^{+} cells in *Pten*$^{+/-}$*Myc*$^{-/-}$ and *Pten*$^{-/-}$*Myc*$^{-/-}$ mice are relatively larger in size, suggesting that they are megakaryocytes.



Supplementary Data 8. Reduction of thymocyte numbers in thymus glands of *Pten*$^{+/-}$*Myc*$^{-/-}$ and *Pten*$^{-/-}$*Myc*$^{-/-}$ mice. **A.** Total mononucleated cell numbers (MNCs) in thymus glands of WT, *Pten*$^{-/-}$*Myc*$^{+/-}$, *Pten*$^{+/-}$*Myc*$^{-/-}$ and *Pten*$^{-/-}$*Myc*$^{-/-}$ mice. **B.** CD4 and CD8 staining and flow cytometric analysis of thymocytes in the thymuses of mutant mice.