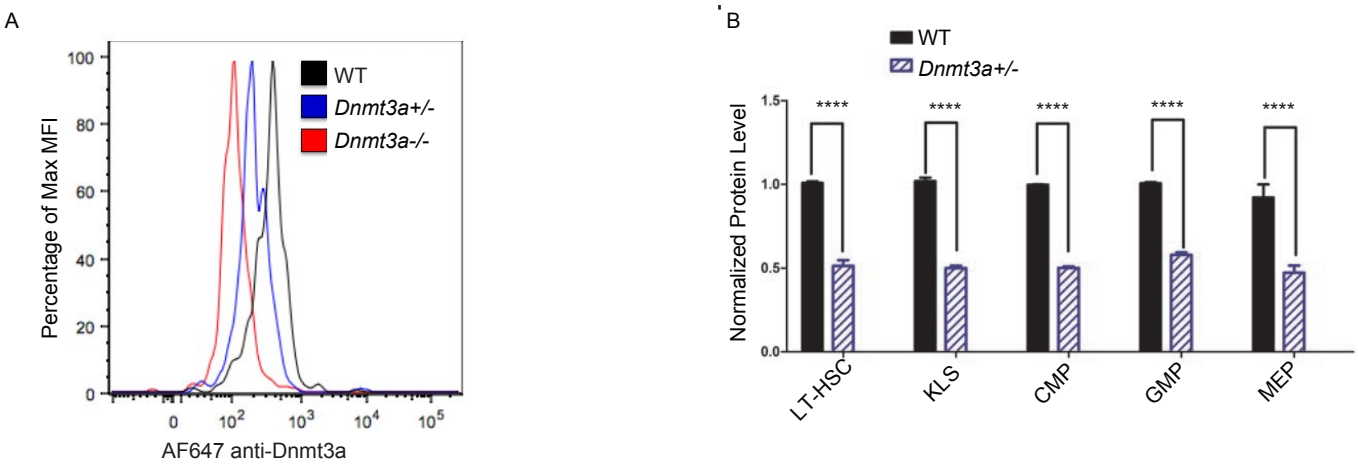
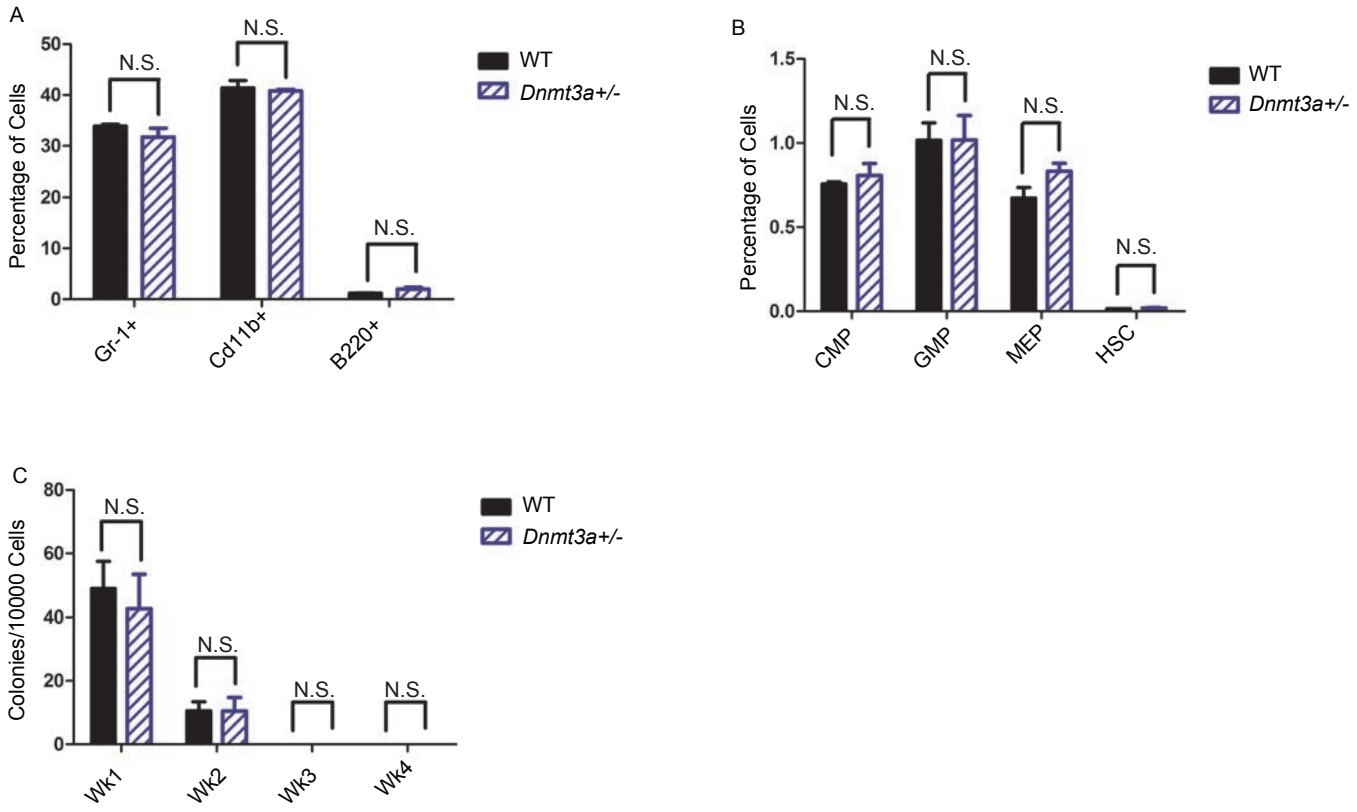
Supplemental Figure 1



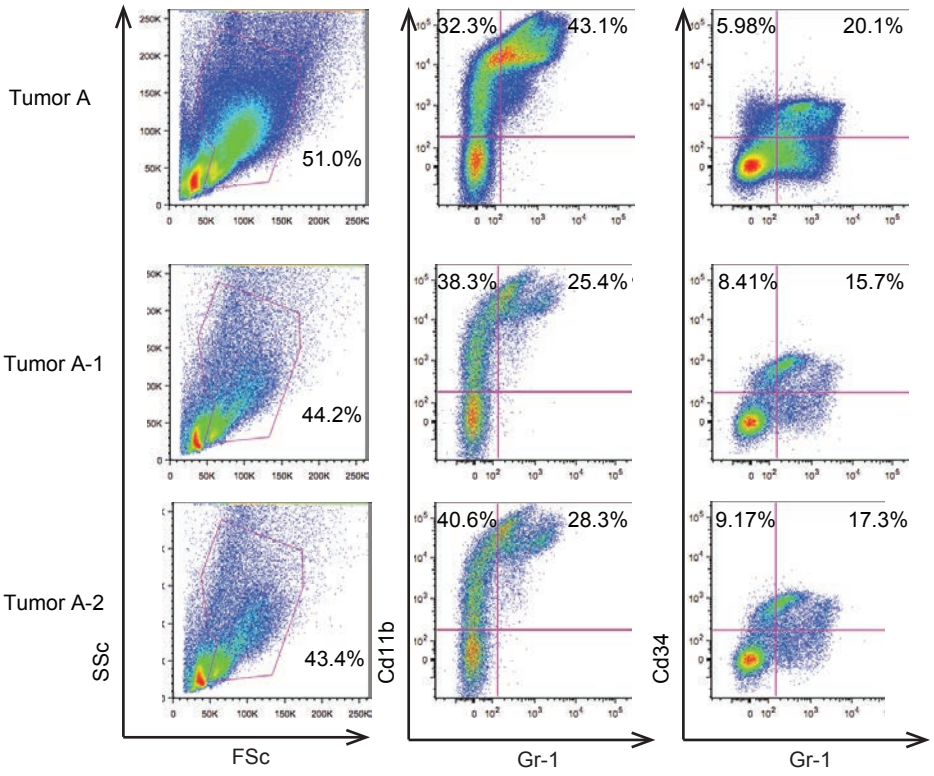
Supplemental Figure 1. Dnmt3a protein levels are reduced by ~50% in the stem and progenitor compartments of *Dnmt3a*$^{+/-}$ mice. (A) – (B) Cells from the indicated stem and progenitor compartments were harvested from two-week old *Dnmt3a*$^{+/+}$, *Dnmt3a*$^{+/-}$, and *Dnmt3a*$^{-/-}$ mice for intracellular flow cytometry. (A) Representative MFI histogram of Dnmt3a levels is shown for the KLS-SLAM compartment in *Dnmt3a*$^{+/+}$, *Dnmt3a*$^{+/-}$, and *Dnmt3a*$^{-/-}$ mice. (B) Quantification of Dnmt3a levels in the indicated compartments of Dnmt3a+/+ versus *Dnmt3a*$^{+/-}$ mice, normalized to *Dnmt3a*$^{+/+}$ expression level (n = 3-5). **** denotes $p < 0.0001$ by two-tailed, unpaired t-test.

Supplemental Figure 2



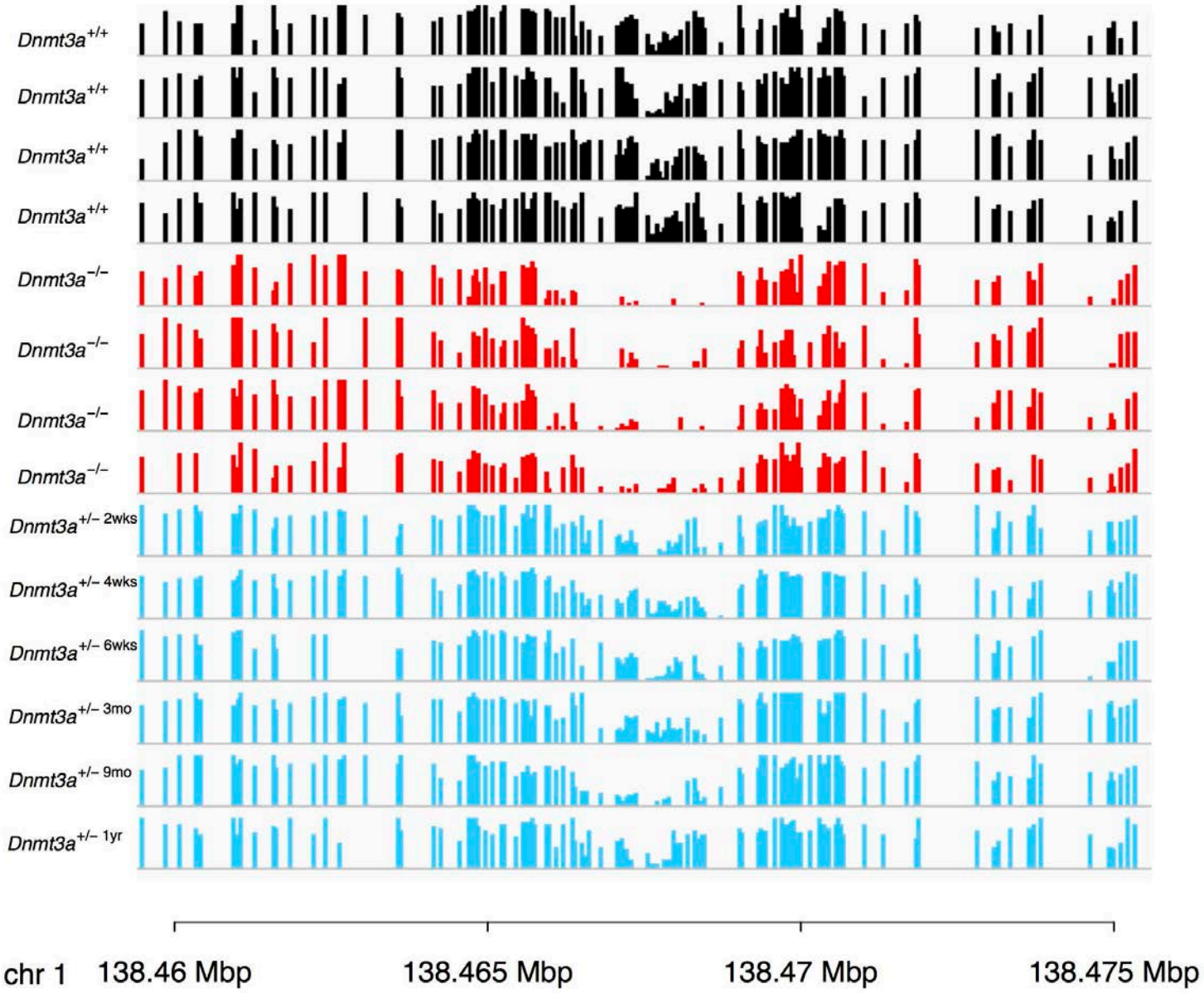
Supplemental Figure 2. Normal hematopoiesis in young *Dnmt3a*$^{+/-}$ mice.
(A) Quantification of myeloid cells (Gr-1+), B220+ B cells, and CD3+ T cells in the bone marrow of six-week old *Dnmt3a*$^{+/+}$ and *Dnmt3a*$^{+/-}$ mice. (B) Quantification of myeloid progenitor compartments (GMP, CMP, MEP) and KLS-SLAM cells (HSC) from young mice, as in (A). (C) Bone marrow from six-week old mice was plated in Methocult media containing IL-3, IL-6 and SCF, and replated every seven days. Quantification of colony numbers demonstrates that *Dnmt3a*$^{+/-}$ cells have no aberrant self-renewal phenotype ex vivo. N.S. not significant by two-tailed, unpaired t-test.

Supplemental Figure 3



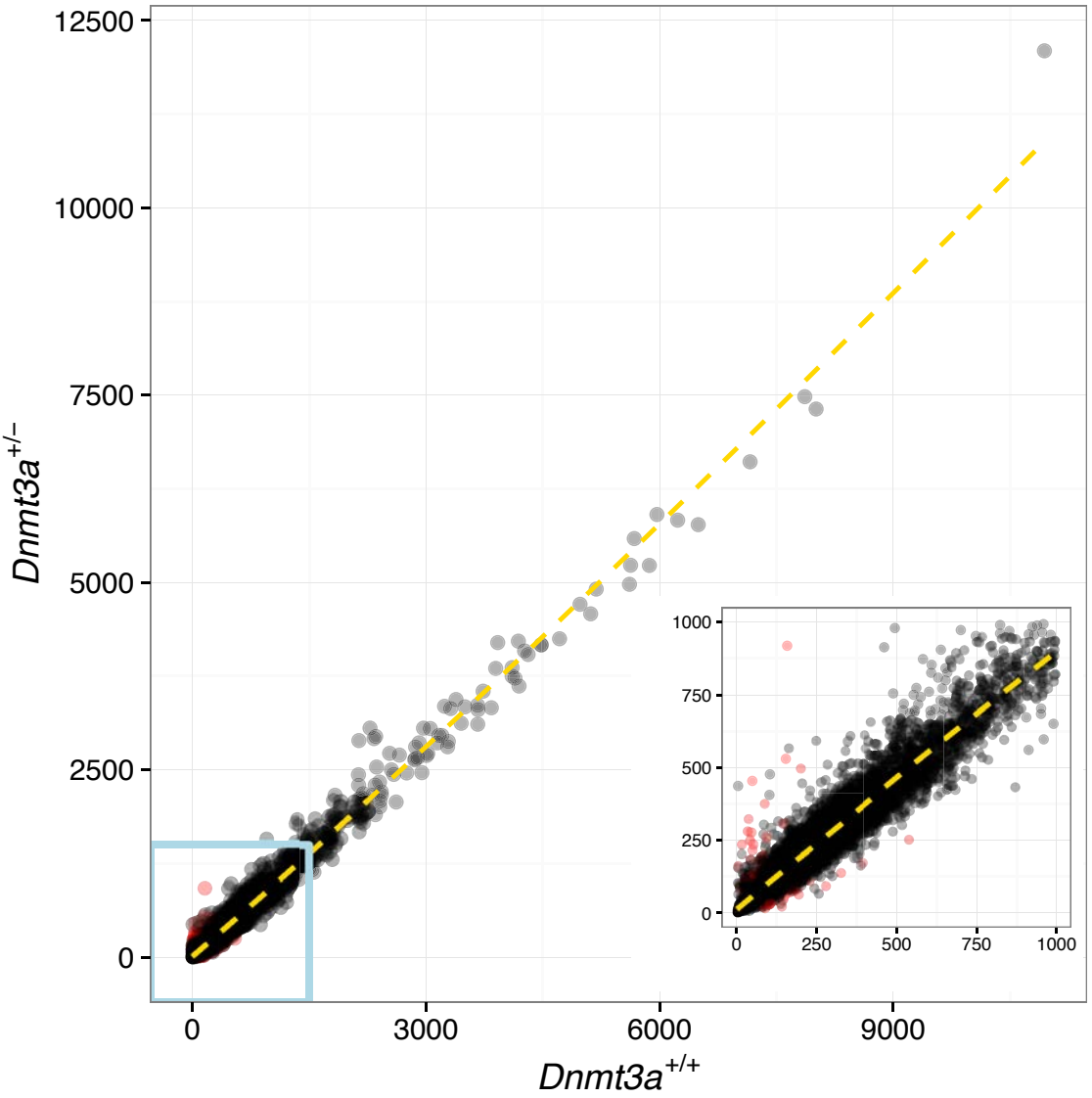
Supplemental Figure 3. Representative flow phenotyping demonstrates secondary tumors recapitulate the immunophenotypes of the primary tumor. Flow cytometry for the indicated markers was performed on tumor A, and two secondary tumors derived from tumor A.

Supplemental Figure 4



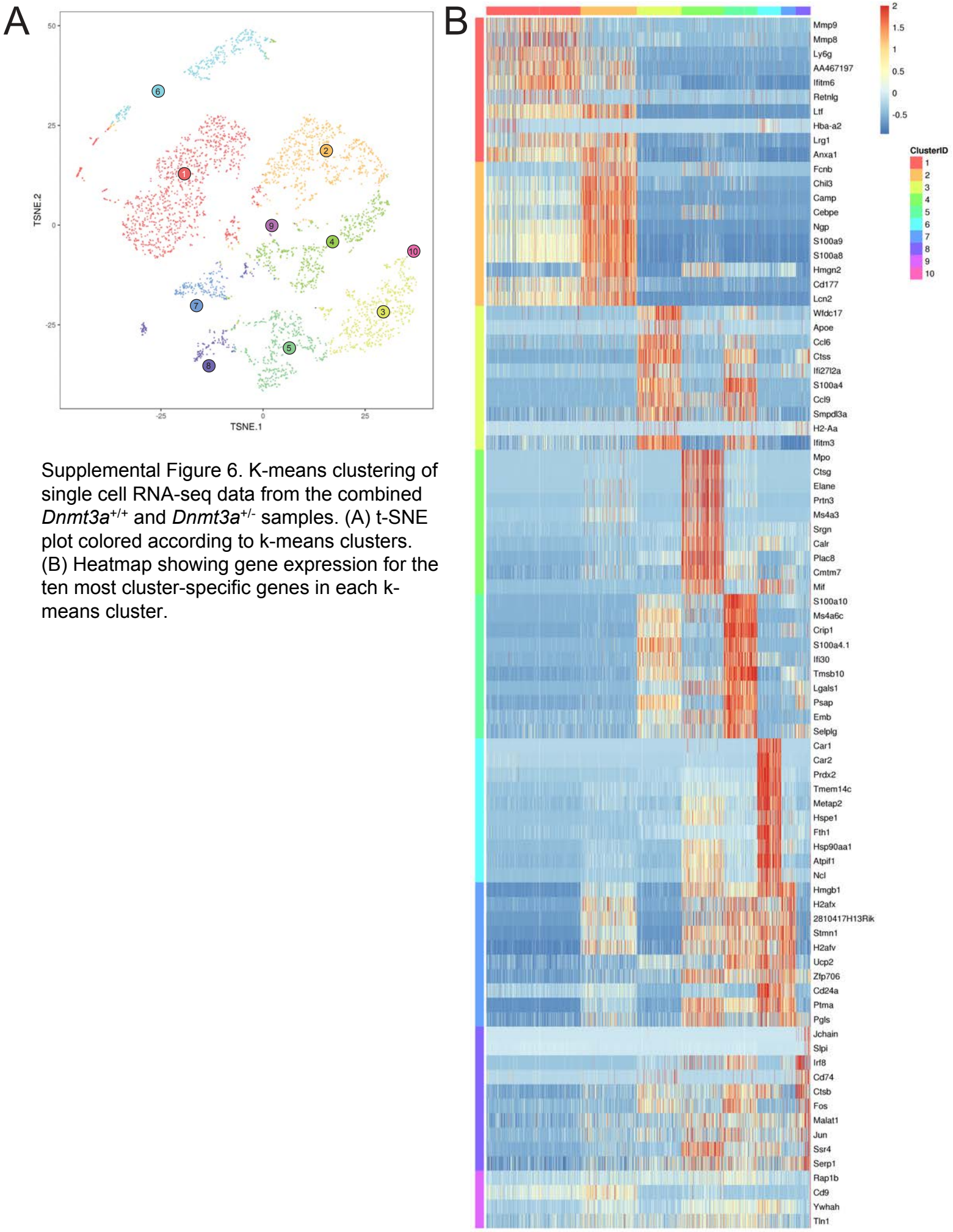
Supplemental Figure 4. CpG methylation values for a region containing a DMR that was hypomethylated in both *Dnmt3a*$^{-/-}$ and *Dnmt3a*$^{+/-}$ samples. Methylation values for each CpG (shown as a bar from 0-100% methylated for each sample) in a *Dnmt3a*$^{-/-}$ hypomethylated DMR located in an intergenic region on chromosome 1. This DMR was also significantly hypomethylated in the *Dnmt3a*$^{+/-}$ samples ($p<0.01$, by a two-tailed, unpaired t-test).

Supplemental Figure 5



Supplemental Figure 5. Comparisons of expression values from the KLS cells of *Dnmt3a*$^{+/+}$ and *Dnmt3a*$^{+/-}$ mice. Plot of the average expression values for all annotated genes from the mouse Exon 1.0 array from KLS cells purified from the bone marrow of six-week old Dnmt3a$^{+/+}$ mice (X axis, n = 3) or *Dnmt3a*$^{+/-}$ mice (Y axis, n = 3). Red indicates a value that was significantly different in a 2-way ANOVA test.

Supplemental Figure 6



Supplemental Figure 6. K-means clustering of single cell RNA-seq data from the combined *Dnmt3a*$^{+/+}$ and *Dnmt3a*$^{+/-}$ samples. (A) t-SNE plot colored according to k-means clusters. (B) Heatmap showing gene expression for the ten most cluster-specific genes in each k-means cluster.