

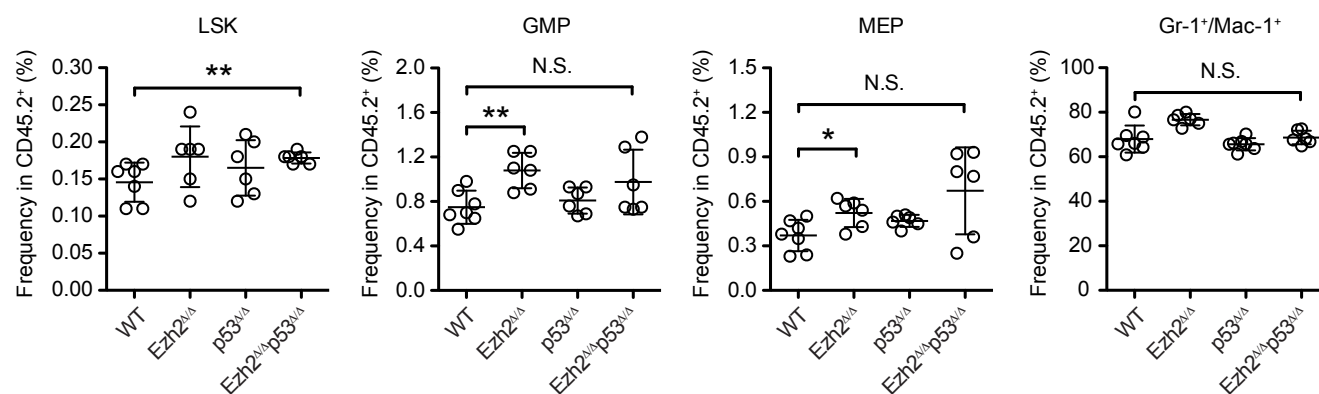


Figure S1: Flowcytometric analysis of hematopoietic stem/progenitor cells and mature myeloid cells in the BM

Proportions of Lineage⁻Sca-1⁺c-Kit⁺ (LSK) cells, GMP (Lineage⁻Sca-1⁺FcγR⁺CD34⁺) cells, MEP (Lineage⁻Sca-1⁺FcγR⁻CD34⁻) cells and mature myeloid cells (Gr-1⁺ and/or Mac-1⁺) among CD45.2⁺ hematopoietic cells in BM. Bars show the mean ± SEM (n=6-7), *p<0.05, and **p<0.01 by the Student's t-test or the Mann-Whitney U-test. N.S. stands for not significant.

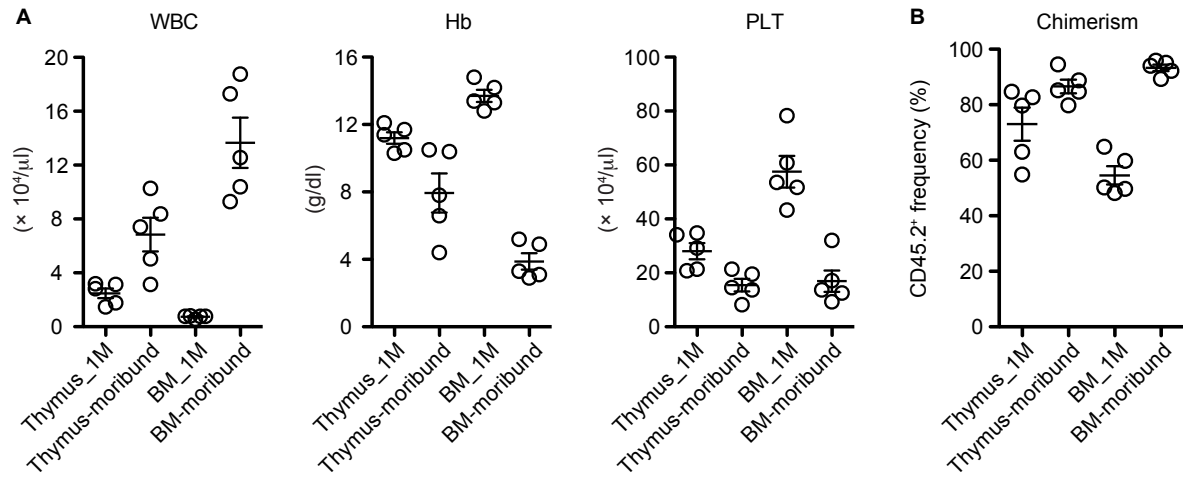


Figure S2: Complete blood counts and chimerism in the secondary transplanted mice

A) Complete blood cell counts of BM cells- and thymocytes-transplanted mice (CD45.1⁺) one month after transplantation (n=5) and moribund ETP-ALL mice at the time of sacrifice (n=5). B) Proportions of CD45.2⁺ donor-derived hematopoietic cells in the PB. Bars show the mean $\pm$ SEM.

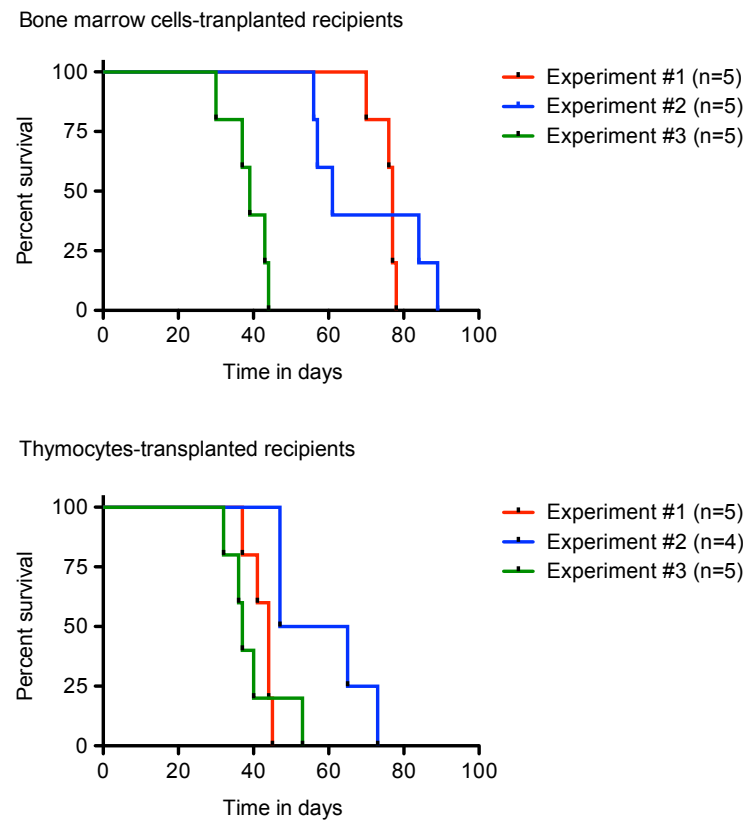


Figure S3: Shorter survivals of the secondary-transplanted mice performed by three independent experiments

Canonical PRC2 target genes

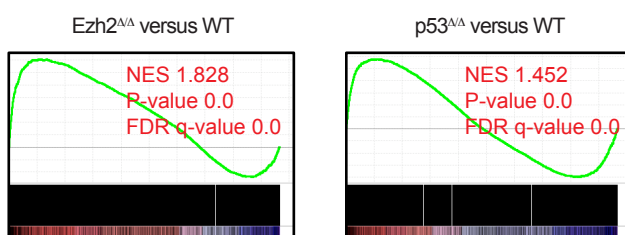
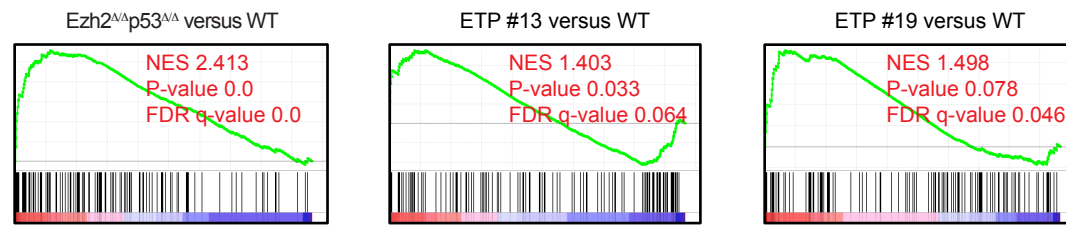


Figure S4: GSEA plots for canonical PRC2 target genes.

Normalized enrichment score (NES), nominal p value (P-value), and false discovery rate (FDR) q-values are indicated.

RAS signaling pathway genes



JAK-STAT signaling pathway genes

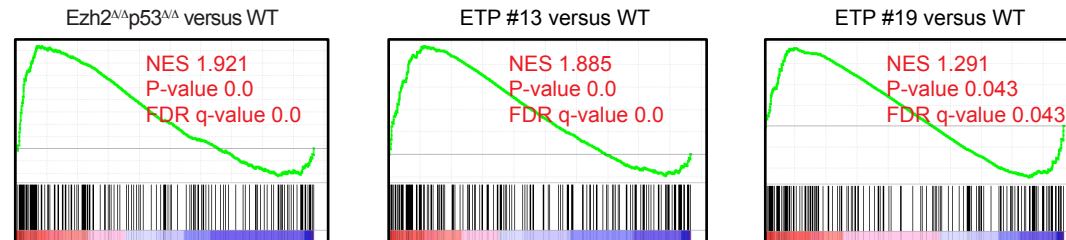


Figure S5: GSEA plots for JAK-STAT signaling pathway genes (WIERENGA_STAT5A_TARGETS_UP) and RAS signaling pathway genes (CHIARADONNA_NEOPLASTIC_TRANSFORMATION_KRAS_UP). Normalized enrichment score (NES), nominal p value (P-value), and false discovery rate (FDR) q-values are indicated.

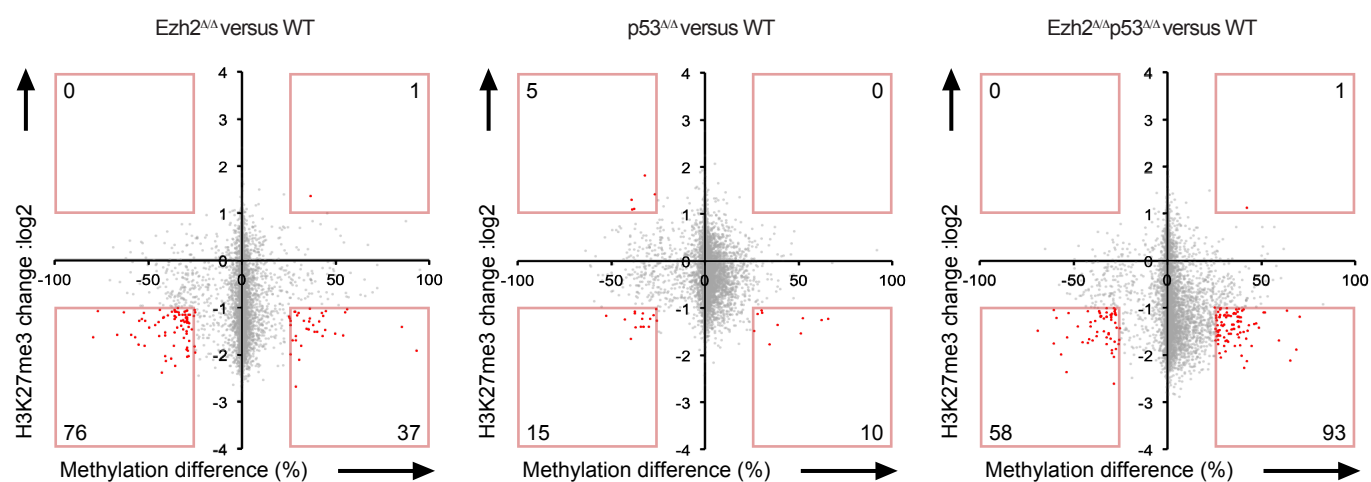


Figure S6: Correlation between the levels of DNA methylation and H3K27me3 in DN cells

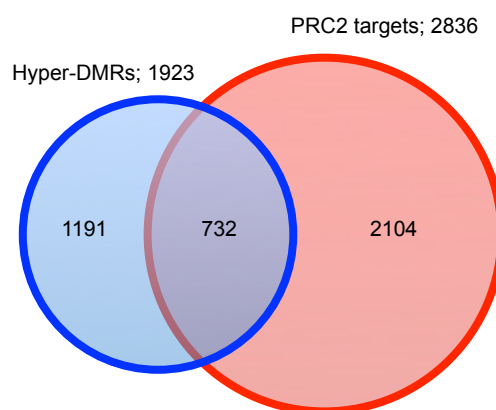


Figure S7: Overlap between hyper-DMRs and PRC2 target genes in $Ezh2^{AA}p53^{AA}$ leukemic cells

Figure S8

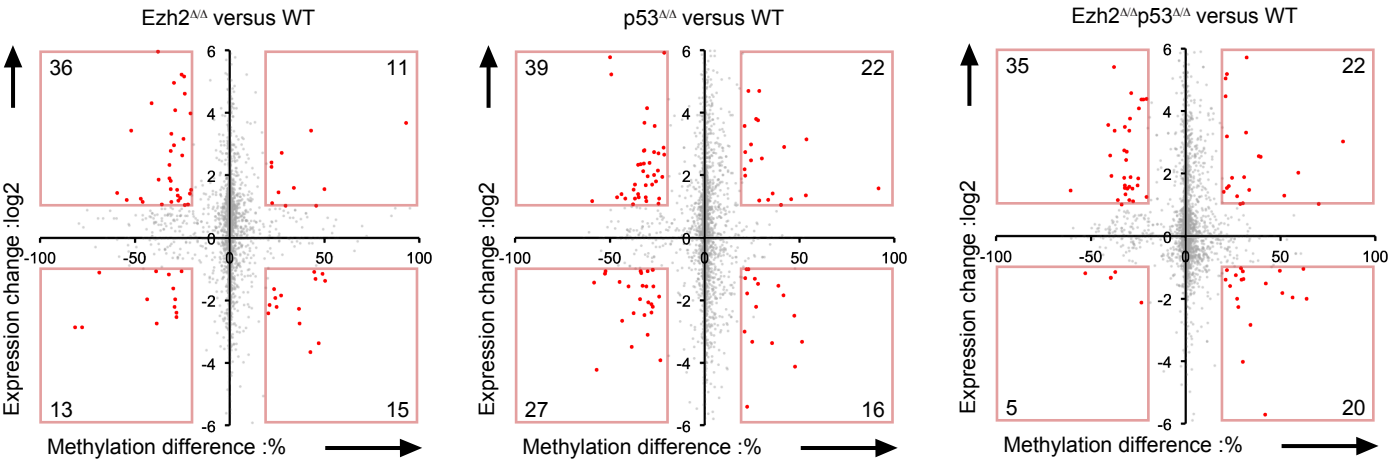


Figure S8: Correlation between the levels of DNA methylation and gene expression in DN2 cells

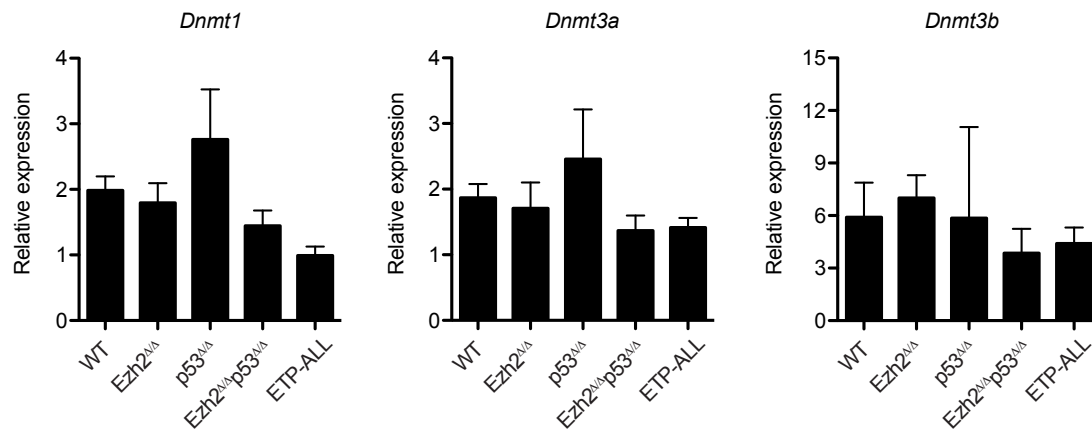


Figure S9: Expression levels of *Dnmt1*, *Dnmt3a*, and *Dnmt3b* in DN2 cells

Quantitative RT-PCR analysis of the expression of *Dnmt* in DN2 cells isolated from WT (n=12), *Ezh2*^{Δ/Δ} (n=6), *p53*^{Δ/Δ} (n=6), and *Ezh2*^{Δ/Δ}/*p53*^{Δ/Δ} (n=8) mice 3 months after transplantation and *Ezh2*^{Δ/Δ}/*p53*^{Δ/Δ} ETP-ALL mice (n=8). Bars show the mean ± SEM

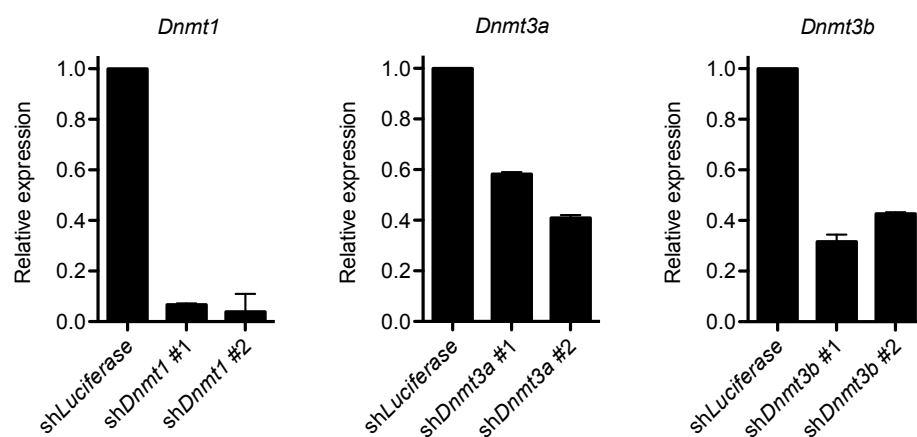


Figure S10: Expression levels of *Dnmt* in shRNA-directed *Dnmt*-vector-transduced cells

Quantitative RT-PCR analysis of the expression of *Dnmt1*, *Dnmt3a* and *Dnmt3b* in shRNA vector-transduced 32D cells. *Gapdh* was used to normalize the amount of input RNA. Data are shown as the mean $\pm$ SD (n=3).

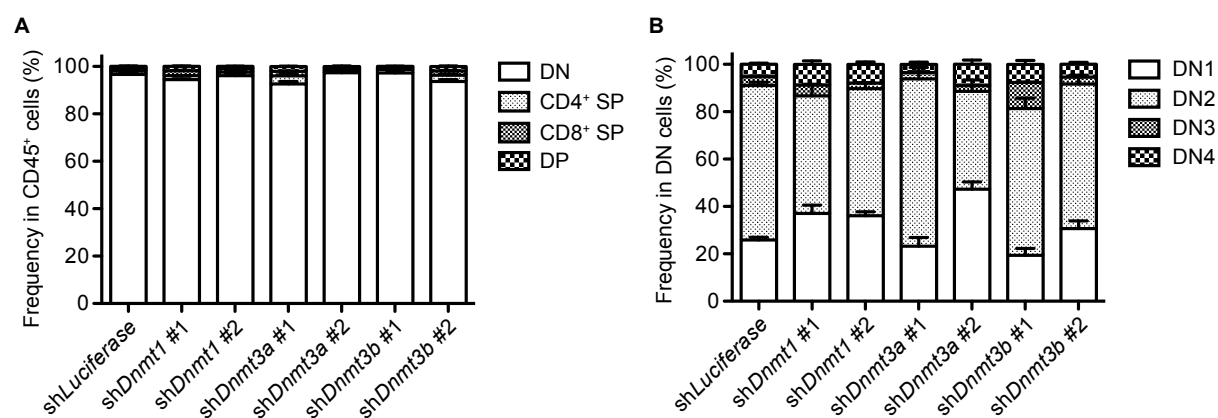


Figure S11: Flowcytometric profiles in Dnmt knockdown ETP-ALL cells

ETP leukemic cells were transduced with individual Dnmt knockdown vectors, and GFP⁺ transduced cells were subjected to culture on Tst4/DLL1 stromal cells in the presence of SCF, IL7, and Flt3L for 9 days.

A) Proportions of DN, CD4⁺ SP, CD8⁺ SP, and DP cells in GFP⁺ transduced leukemic cells on day 9 of the culture.

B) Proportions of DN1, DN2, DN3, and DN4 cells in CD4⁺CD8⁺GFP⁺ transduced leukemic cells on day 9 of the culture.

Two independent experiments were performed. Data are shown as the mean $\pm$ SD (n=4).