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## Supplemental information

### **Somatic *Dnmt3a* inactivation leads to slow, canonical DNA methylation loss in murine hematopoietic cells**

**Amanda M. Smith, Angela M. Verdoni, Haley J. Abel, David Y. Chen, Shamika Ketkar, Elizabeth R. Leight, Christopher A. Miller, and Timothy J. Ley**

**Supplemental Figures for: Somatic *Dnmt3a* inactivation leads to slow, canonical DNA methylation loss in murine hematopoietic cells**

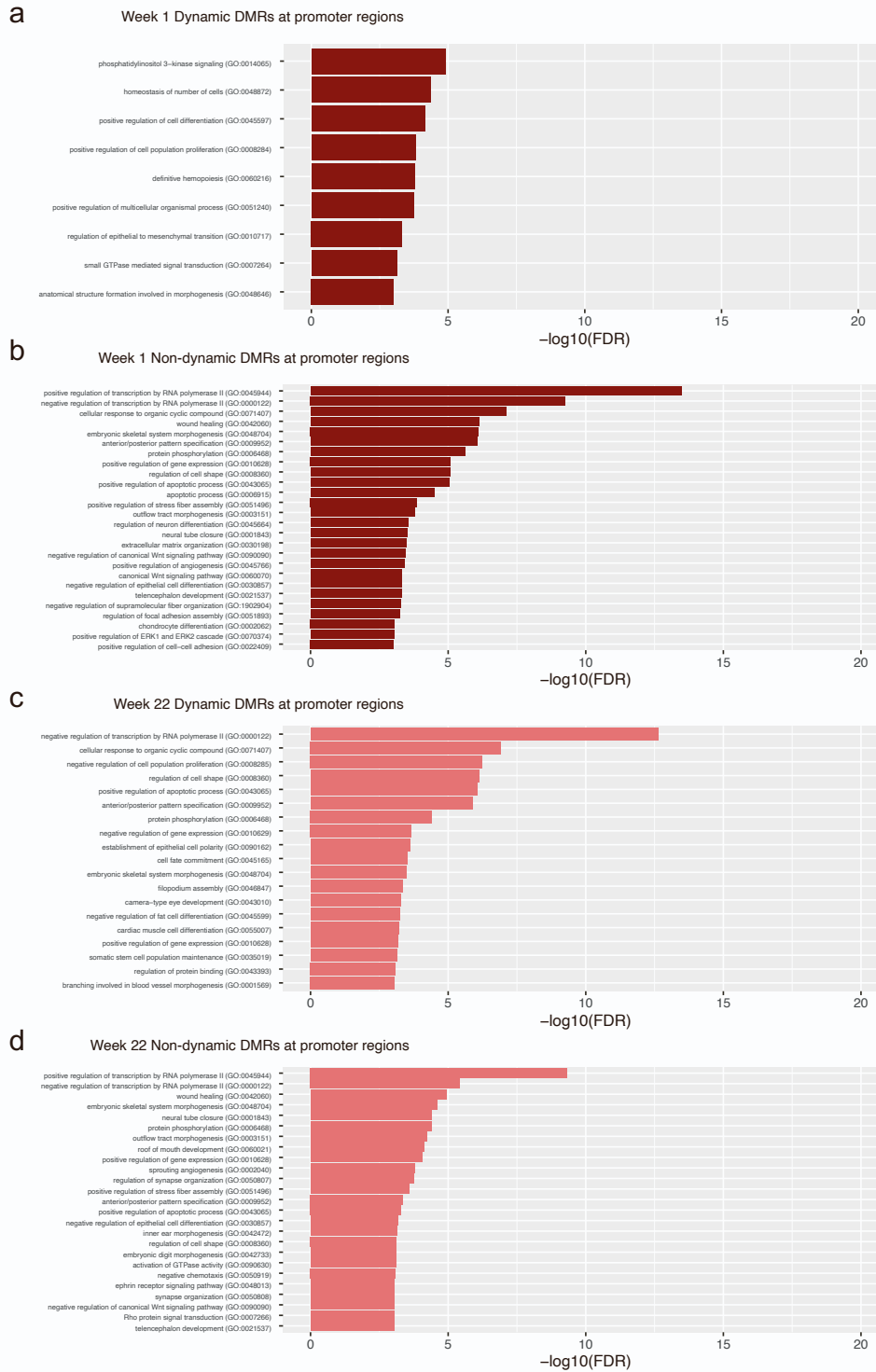
Amanda M. Smith<sup>a\*</sup>, Angela M. Verdoni<sup>a,1\*</sup>, Haley J. Abel<sup>a</sup>, David Y. Chen<sup>b</sup>, Shamika Ketkar<sup>a,2</sup>, Elizabeth R. Leight<sup>a,3</sup>, Christopher A. Miller<sup>a</sup>, and Timothy J. Ley<sup>a</sup>.



Supplementary Figure 1

**Supplementary Figure 1. GO annotations for dynamic and non-dynamic DMRs located within or near genes (related to Figure 4 and Supplemental Table 3)**

Gene ontology enrichment analysis, using genes associated with DMRs (within a gene promoter, gene body, or within 10 kb of a gene). Terms with FDR < 0.001 are shown. a) Enriched terms from DMRs with dynamic (rapid) methylation changes (as defined in the text) at week 1 in the takeaway samples. b) Enriched terms from DMRs with non-dynamic (slow/absent) methylation changes at week 1 in the takeaway samples a) Enriched terms from DMRs with dynamic (rapid) methylation changes at week 22 in the takeaway samples. b) Enriched terms from DMRs with non-dynamic (slow/absent) methylation changes at week 22 in the takeaway samples. GO enrichment analysis was performed with PANTHER (<http://pantherdb.org>, PMID: 30804569) using Fisher's Exact Test and FDR correction.

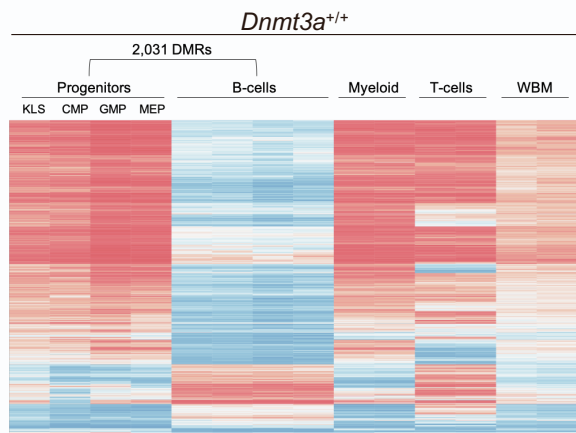


Supplementary Figure 2

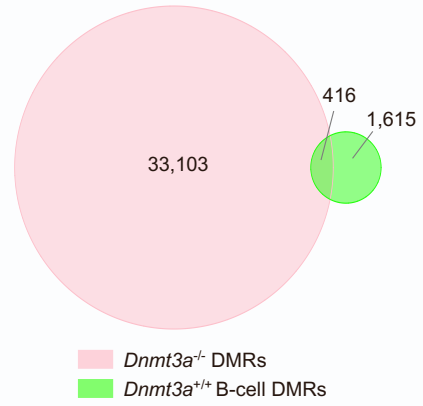
**Supplementary Figure 2. GO annotations for dynamic and non-dynamic DMRs associated with gene promoters only (related to Figure 4 and Supplemental Table 3)**

Gene ontology enrichment analysis, using genes associated with DMRs, requiring the DMR to intersect a gene promoter. Terms with FDR < 0.001 are shown. a) Enriched terms from DMRs with dynamic (rapid) methylation changes (as defined in the text) at week 1 in the takeaway samples. b) Enriched terms from DMRs with non-dynamic (slow/absent) methylation changes at week 1 in the takeaway samples a) Enriched terms from DMRs with dynamic (rapid) methylation changes at week 22 in the takeaway samples. b) Enriched terms from DMRs with non-dynamic (slow/absent) methylation changes at week 22 in the takeaway samples. GO enrichment analysis was performed as described for Supplemental Figure 1.

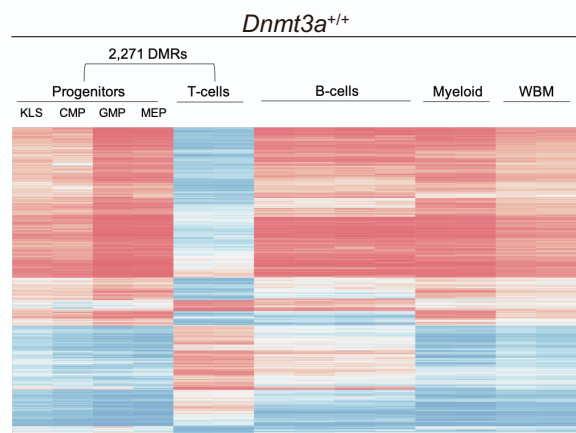
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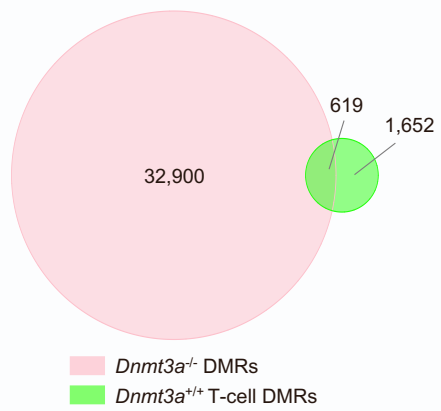
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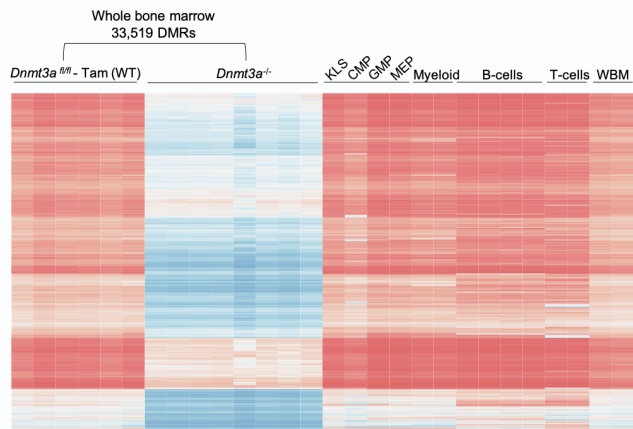
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d



e

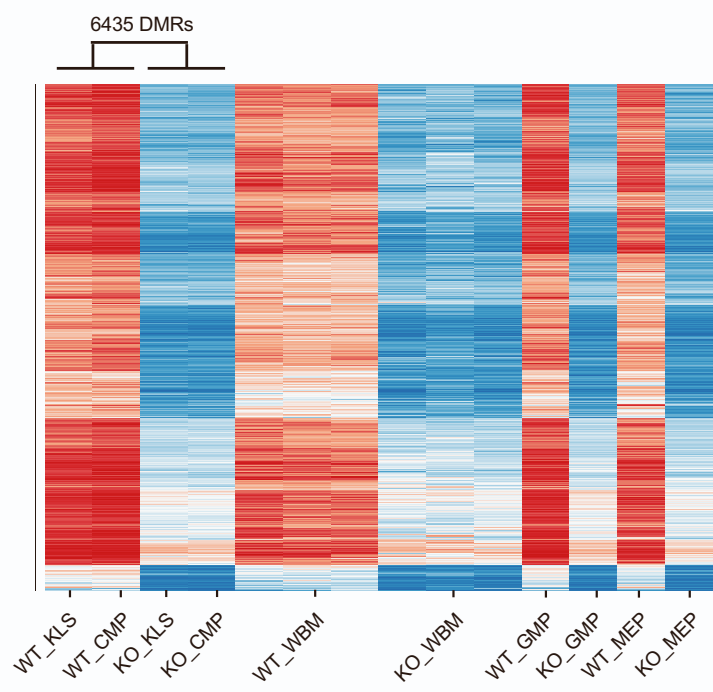


Supplementary Figure 3

**Supplementary Figure 3. Differential methylation and expression signatures in hematopoietic progenitors and mature lymphoid cells (related to Figure 5)**

- a) Heatmap of mean methylation levels for DMRs identified by comparing progenitors (KLS, MEP, CMP and GMP) and B-cells (CD19+B220+) enriched by FACS sorting. Methylation values for those DMRs in myeloid, T-cells and whole bone marrow are passively plotted.
- b) Venn diagram showing overlap of the 33,519 DMRs defined in *Dnmt3a*<sup>-/-</sup> bone marrow (pink) vs. DMRs defined for the 2,031 *Dnmt3a*<sup>+/+</sup> B-cells (green).
- c) Heatmap of mean methylation levels for DMRs identified by comparing progenitors (KLS, MEP, CMP and GMP) vs. T-cells (CD3e+) enriched by FACS sorting. Methylation values for those DMRs in myeloid, B-cells and whole bone marrow are passively plotted.
- d) Venn diagram showing overlap of the 33,519 DMRs defined in *Dnmt3a*<sup>-/-</sup> bone marrow (pink) vs. DMRs defined for the 2,271 *Dnmt3a*<sup>+/+</sup> T-cells (green).
- e) Heatmap of mean methylation levels for 33,519 *Dnmt3a*<sup>-/-</sup> dependent DMRs with passive plotting for progenitors (KLS, MEP, CMP and GMP), mature myeloid cells (CD11b+/Gr1+), B-cells (CD19+B220+), T-cells (CD3e+) and whole bone marrow (WBM).





Supplementary Figure 4

**Supplementary Figure 4. DMRs defined in early progenitor populations persist in terminally differentiated bone marrow cells (related to Figure 5)**

Heatmap of mean methylation values for 6,435 DMRs identified by comparing WT vs *Dnmt3a* KO flow-purified progenitor cell populations (KLS and CMP; pooled for this analysis). Methylation values for the same DMRs are passively plotted in both WT and *Dnmt3* KO samples, from whole bone marrow and more committed progenitor cell populations (GMP and MEP).