



Figure S4. Hematopoietic abnormalities were observed in *Setd2* deficiency mice at about 8 months after pl-pC induction.

(A) Representative images of blood smears. WT=2 and KO=4. Triangle indicates teardrop cell. (B-C) Follow-up of the routine blood test at indicated time points. n=10. B: PLT; C: WBC. (D) Proportion follow-up of different cell lineages in KO PB relative to WT control at indicated time points. n=10. (E) Survival curve of WT and KO mice. n=10. (F) Phenotype analysis of spleen and liver. Left: Morphology of spleen and liver; Middle: Body index (the ratio of spleen or liver to body weight), n=4; Right: Cell count of total spleen cells. n=3. (G) Representative images of Giemsa staining of spleen touch section. (H) Proportion analysis of different cell lineages in KO spleen relative to

WT control. n=3. (I) Representative images of Haematoxylin-eosin (HE) staining of spleen tissue sections. (J) Proportion analysis of different cell lineages in BM. n=3. (K) Representative images of Haematoxylin-eosin (HE) staining of liver tissue sections. (L) Representative images of CD45 immunohistochemistry of liver tissue sections. (M) Morphology (left) and the absolute BM cell count (right) of two femurs and tibias. n=3. (N) Giemsa staining of BM smears (left) and myeloid: erythroid ratio analysis (right). n=3. (O) Representative images of HE staining of BM tissue sections. (P-Q) Representative images of silver staining of BM (P) and spleen (Q) tissue sections. (R) FACS analysis of EGFP positive cells in BM CD45⁺Ter119⁻ cells. n=3. (S) Cell counting analysis of HSPC subsets in KO BM relative to that in WT control. n=3. (T) FACS analysis of HSPCs in KO spleen relative to that in WT control. n=3. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.