



Figure S3. BM transplantation assays evaluate the critical inference of *Setd2* for murine HSC self-renewal and differentiation.

(A) Experiment schematic for competitive BM transplantation (cBMT). (B) Representative FACS analysis of donor-derived cell proportion (CD45.2) in PB of cBMT mice at 16 weeks after transplantation. (C-E) Statistical comparison of donor-derived cell proportion in different PB cell lineages (C: B cells, D: T cells, E:

myeloid cells) between WT and KO cBMT mice at indicated time points. n=16. (F) Proportion analysis of different cell lineages in donor-derived PB cells from WT and KO cBMT mice at indicated time points. n=16. (G) Representative FACS analysis of homing cells (CD45.2) at 6 hours and 18 hours after transplantation. (H) Proportion analysis of homing cells (CD45.2) at 6 hours (n=3) and 18 hours (n=4) after transplantation. (I) Experiment schematic for serial non-competitive BM transplantation (ncBMT). (J) Proportion analysis of donor-derived cells in different PB cell lineages of primary (WT=19, KO=18) and secondary (n=14) ncBMT mice at 16 weeks after transplantation. (K) Representative FACS image of donor-derived LT-HSCs in primary and secondary ncBMT mice. (L) Proportion analysis of different cell lineages in donor-derived PB cells of primary (WT=19, KO=18) and secondary (n=14) ncBMT mice at 16 weeks after transplantation. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.