

**Figure S1. Quantification of total BM nucleated cells isolated from 2 months old wild-type and *Pot1b*<sup>Δ/Δ</sup> mice.** n=5; P=0.30.

**Figure S2. Aged *Pot1b*<sup>Δ/Δ</sup> mice develop pancytopenia in their peripheral blood.** Peripheral blood parameters from four 15 months old wild-type and six *Pot1b*<sup>Δ/Δ</sup> mice were analyzed. (A) White blood cell count (WBC x 10<sup>3</sup>/uL; wild-type vs. *Pot1b*<sup>Δ/Δ</sup> mice, P=3.0 x10<sup>-4</sup>). (B) Hemoglobin (g/dL; wild-type vs. *Pot1b*<sup>Δ/Δ</sup> mice, P=5.0 x10<sup>-3</sup>). (C) Platelet count (x 10<sup>3</sup>/uL; wild-type vs. *Pot1b*<sup>Δ/Δ</sup> mice, P=1.1 x10<sup>-4</sup>). The median value for each group is marked by a black bar.

**Figure S3. Annexin V/7-AAD FACS profiles of peripheral blood isolated from 15 months old wild-type and *Pot1b*<sup>Δ/Δ</sup> mice.** The upper panels are representative results showing that the peripheral blood of *Pot1b*<sup>Δ/Δ</sup> mice display an 8-fold increase in the number of apoptotic cells compared to age-matched wild-type controls (54.6% wild-type vs. 6.5% *Pot1b*<sup>Δ/Δ</sup> mice). Lower panel shows individual data from 4 wild-type and 5 *Pot1b*<sup>Δ/Δ</sup> mice (P=1.6 x 10<sup>-3</sup>).

**Figure S4. Increased DNA damage response in *Pot1b*<sup>Δ/Δ</sup> mice.** Cell lysates isolated from three 2 months old wild-type and *Pot1b*<sup>Δ/Δ</sup> lineage negative BM cells were probed with antibodies against phospho-Chk2 (P-Chk2), total Chk2 and p53. Tubulin was used as the loading control.

**Figure S5. Statistical results for FACS analysis of multi-lineage negative population derived from 2, 4, and 6 month old wild-type and *Pot1b*<sup>Δ/Δ</sup>; mTerc<sup>+/-</sup> mice.** Numbers are the percentage of LSK (left) and LK (right) cells in total BM.

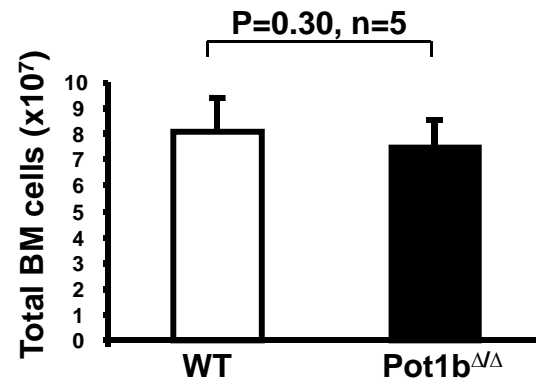


Figure S1

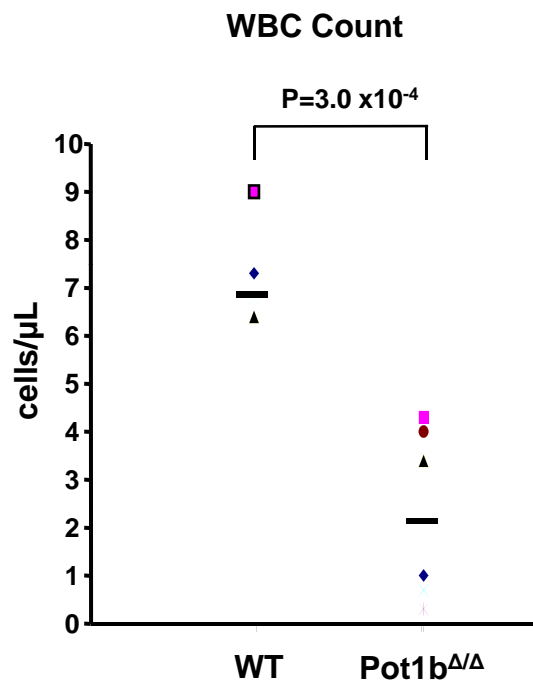
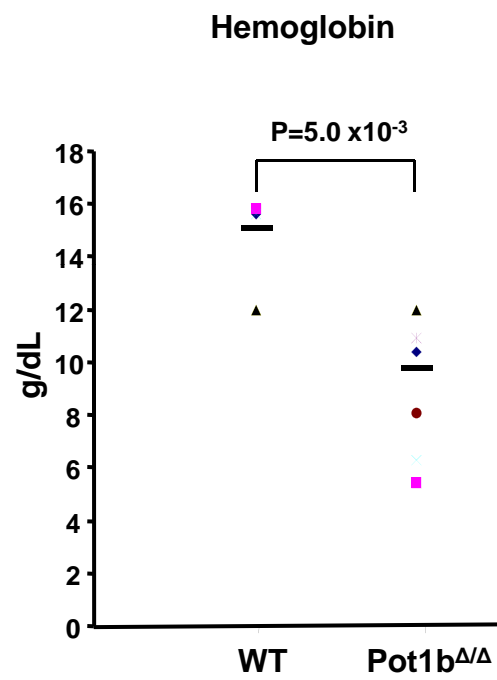
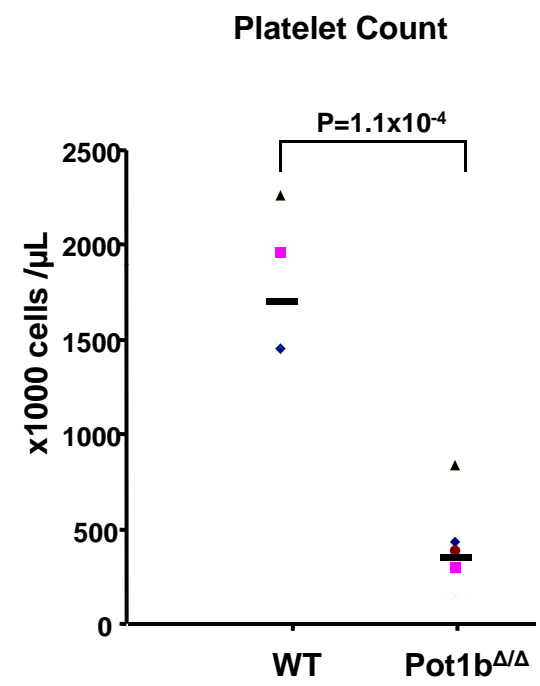
**A****B****C**

Figure S2

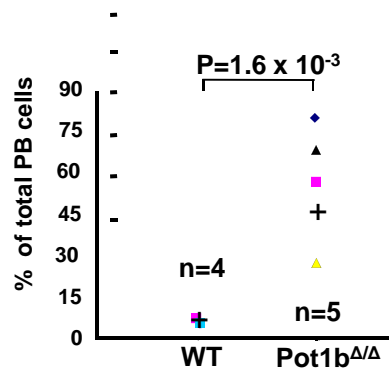
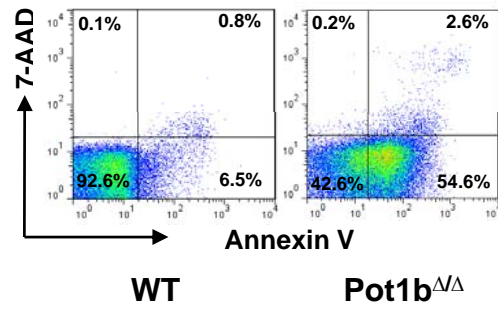


Figure S3

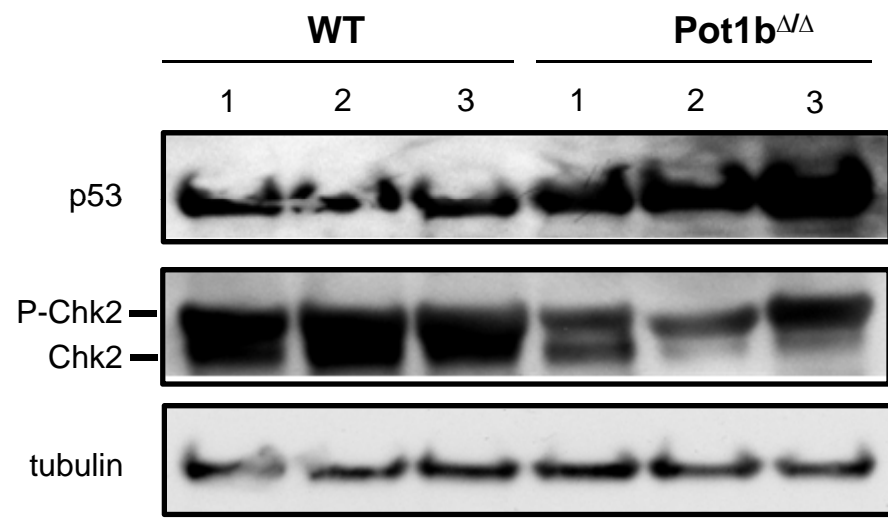


Figure S4

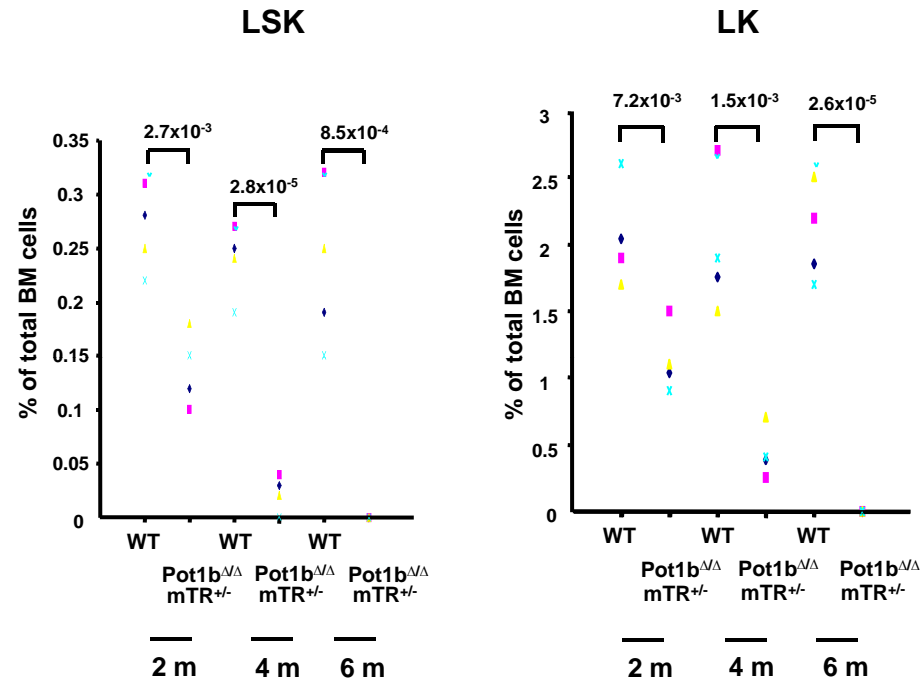


Figure S5