

Supplemental material

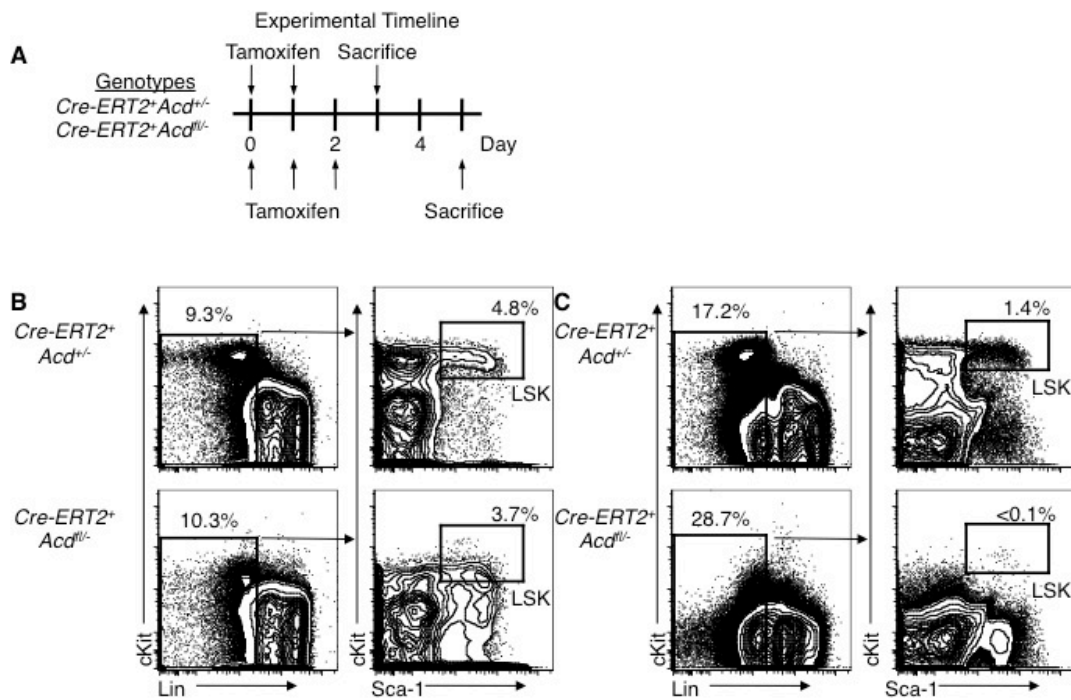


Figure S1. *Acd/Tpp1* inactivation with tamoxifen-inducible Cre recombinase results in rapid depletion of hematopoietic stem and progenitor cells.

(A) Experimental design: tamoxifen was administered to control $Cre-ERT2^+ x Acid^{+/-}$ or $Cre-ERT2^+ x Acid^{fl/-}$ mice (1 mg i.p. daily day 1-3). The $Cre-ERT2$ lentitransgene encodes the ubiquitously expressed Tamoxifen-inducible Cre-ERT2 recombinase; (B-C) Flow cytometric analysis of bone marrow at day 3 (B) or day 5 (C) after initiation of tamoxifen. In $Cre-ERT2^+ x Acid^{fl/-}$ mice, the Lineage⁻Sca-1⁺cKit^{hi} (LSK) compartment (containing hematopoietic stem and progenitor cells) became abnormal within 3 days of tamoxifen administration and was severely depleted within 5 days. Representative flow cytometry plots are shown. Numbers indicate the percentage of cells in each gate.

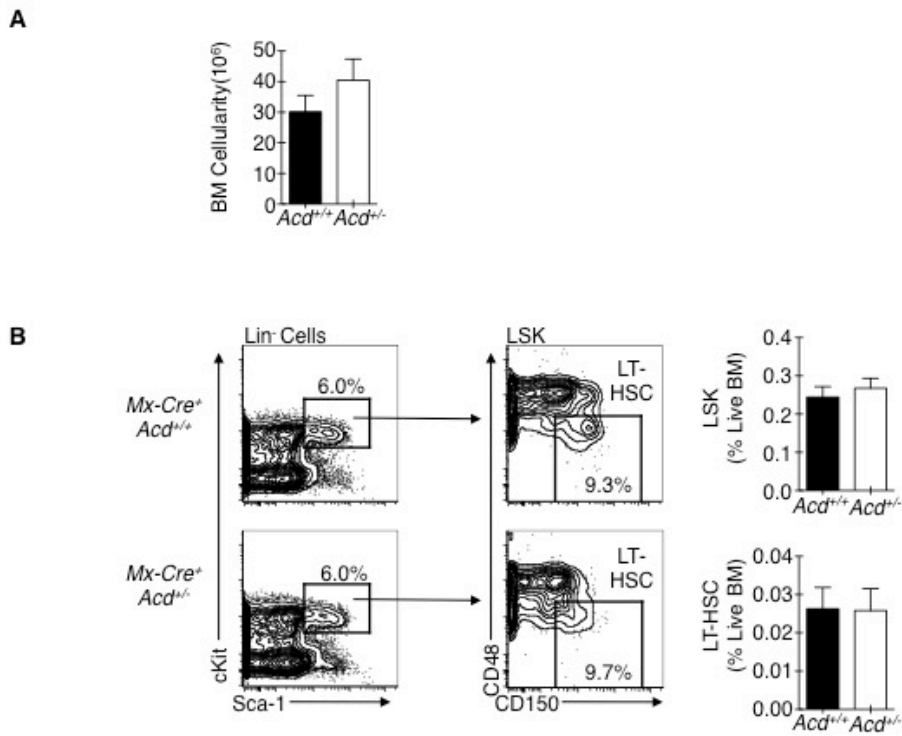


Figure S2. Heterozygosity for the *Acd/Tip1* null allele does not reveal haploinsufficiency.

(**A**) Bone marrow cellularity of wild-type mice compared to *Acd*^{+/-} mice; (**B**) Analysis of the Lin⁻Sca-1^{hi}c-Kit^{hi} LSK and CD150⁺CD48⁻Lin⁻Sca-1^{hi}c-Kit^{hi} long-term HSC (LT-HSC) compartments demonstrating no differences in the frequency of either population in wild-type compared to *Acd*^{+/-} mice (n=4 mice/group, data shown as mean ± SEM). Representative flow cytometry plots are shown. Numbers indicate the percentage of cells in each gate.

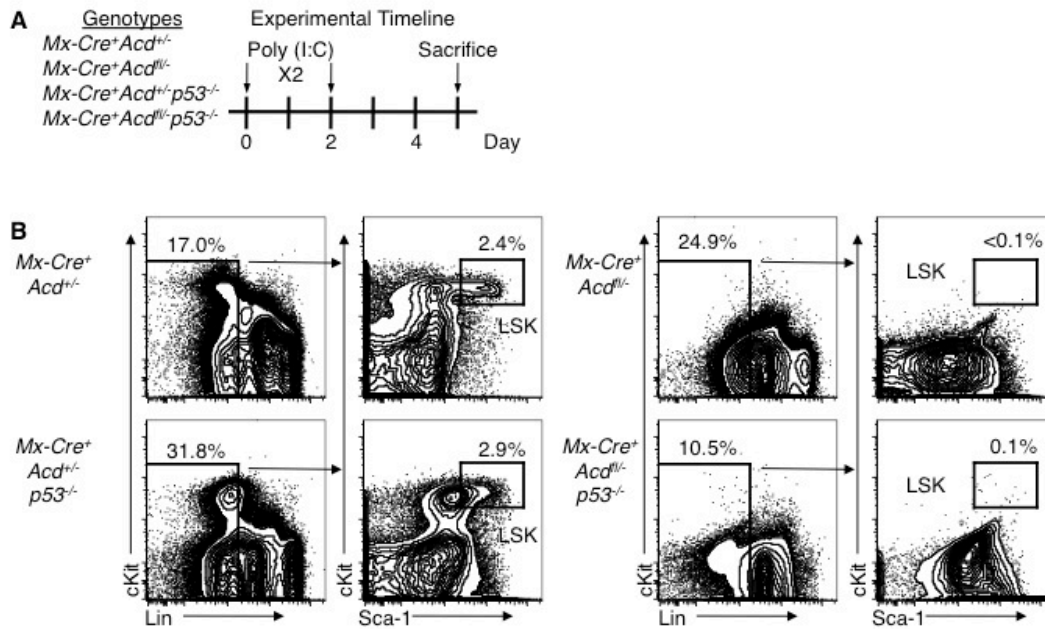


Figure S3. *p53* inactivation does not rescue *Acd/Tpp1*-deficient hematopoietic stem and progenitor cells from acute depletion.

(A) Experimental design: lethally irradiated B6-CD45.1 mice were transplanted with bone marrow from *Mx-Cre⁺Acd^{+/-}p53^{+/+}*, *Mx-Cre⁺Acd^{+/-}p53^{-/-}*, *Mx-Cre⁺Acd^{fl/-}p53^{+/+}* or *Mx-Cre⁺Acd^{fl/-}p53^{-/-}* B6-CD45.2 and wild-type (WT) B6-CD45.1 competitor mice (10^6 cells each). After 6 weeks to allow hematopoietic reconstitution, poly(I:C) was administered; (B) Flow cytometric analysis of bone marrow 5 days after starting poly(I:C) injection, demonstrating an acute depletion of Lineage⁻Sca-1⁺cKit^{hi} (LSK) hematopoietic progenitors in both *Mx-Cre⁺Acd^{fl/-}p53^{+/+}* and *Mx-Cre⁺Acd^{fl/-}p53^{-/-}* recipients (right panels). Representative flow cytometry plots are shown. Numbers indicate the percentage of cells in each gate.