

Figure S1

**Figure S1: Histological analysis of tissue sections from P/R and P/R-FLT3ki leukemic mice.** Paraffin embedded sections were stained with hematoxylin & eosin (H&E). Photographs were taken on a Nikon Eclipse 80i microscope with a Nikon Digital Sight camera using NIS-Elements F4.30 software at a resolution of 2560 × 1920. Using Adobe Photoshop CS2, images were re-sized and set at a resolution of 300 pixels/inch, autocontrast was applied, and unsharp mask was used to improve image clarity. (A,B) Bone marrow sections, scale bar 20  $\mu$ m. (C,D) Spleen sections, scale bar 50  $\mu$ m. (E,F) Kidney sections, scale bar 100  $\mu$ m. (G,H) Liver sections, scale bar 50  $\mu$ m.

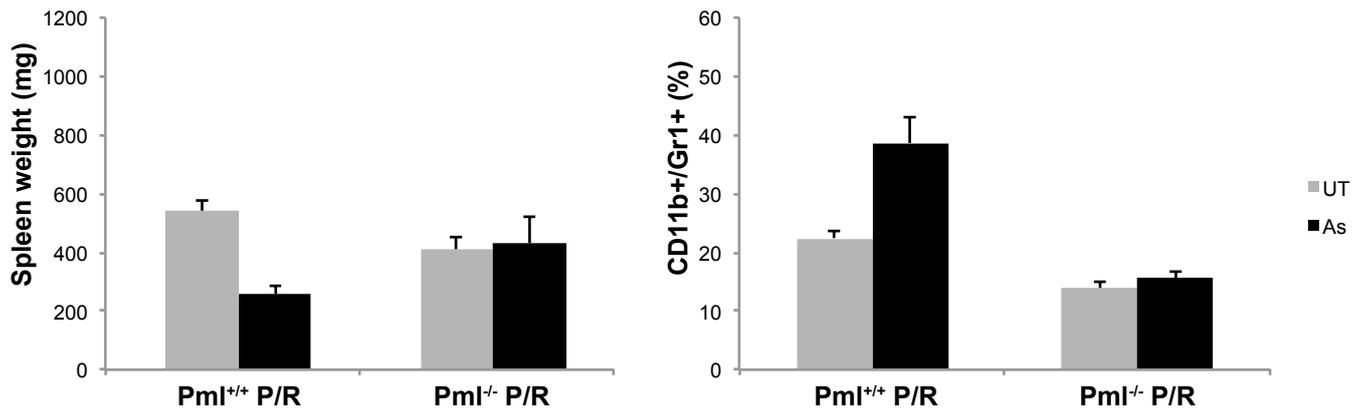


Figure S2

**Figure S2: *Pml*<sup>-/-</sup> APL are resistant to arsenic.** Spleen size (left) and percentage of differentiation (CD11<sup>+</sup>/Gr1<sup>+</sup>, right) of untreated (UT) or As 4-d-treated APL mice in *Pml*<sup>+/+</sup> or *Pml*<sup>-/-</sup> genetic background. Data are expressed as mean ± s.d of independent experiments

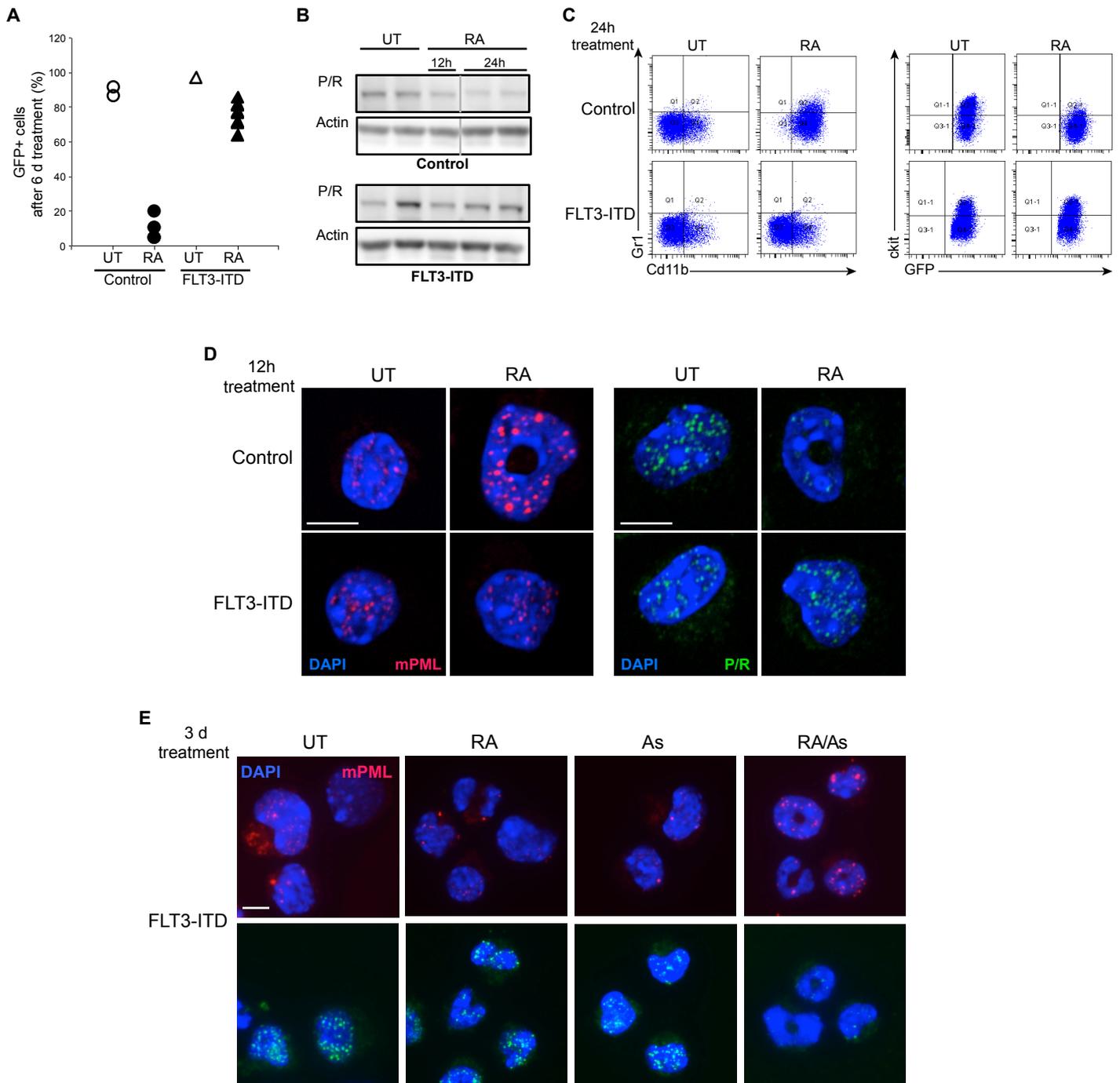


Figure S3

**Figure S3: Overexpression of *FLT3*-ITD in APL cells.** (A) Percentages of GFP-positive APL cells in bone marrow of untreated (UT) or ATRA 6-d-treated (RA) P/R mice (Control, circle) and P/R+*FLT3*-ITD mice (*FLT3*-ITD, triangle). (B) Western blot of PML/RARA (P/R) and Actin expression in the bone marrow of untreated (UT) or ATRA-treated P/R and P/R+*FLT3*-ITD mice. (C) FACS analysis after 24h of in vivo ATRA-treatment of P/R and P/R+*FLT3*-ITD mice. (D) PML NB reformation and PML/RARA degradation assessed by immunofluorescence analysis of murine PML (red) and PML/RARA (green) with DAPI (blue) in bone marrow cells of P/R and P/R+*FLT3*-ITD APL mice 12h-treated with ATRA (scale bar 5  $\mu$ m). (E) Immunofluorescence analysis of murine PML (red) and PML/RARA (green) with DAPI (blue) in bone marrow cells of P/R+*FLT3*-ITD APL mice 3-d-treated with ATRA, As or combined ATRA/As (scale bar 5  $\mu$ m).