**In vitro differentiation of PR bone marrow progenitors.** Bone marrow mononuclear cells from 6-8 week old, 5-FU treated mice were plated in media containing SCF, TPO, IL3 and FLT3 Ligand for 72 hours. Sca1+, Lin- cells were then isolated by high speed cell sorting and replated into media supplemented with SCF and G-CSF. Manual cell counts, flow cytometry and cell cycle analysis by BrdU/7-AAD labeling were performed at serial time points after replating. Data are from 3 separate pools of mice (5-6 mice/genotype).

**ATRA sensitivity assay.** Cryopreserved leukemic spleen cells were thawed at 37° and washed in PBS with 50 μM β-mercaptoethanol and 10% FBS. Cells were plated at 2 x 10^6/ml in RPMI with 15% FCS, 100 ng/ml SCF, 6 ng/ml IL-3, 10 ng/ml IL-6 (Peprotech, Rocky Hill, NJ) ± 1 μM ATRA (Sigma, St. Louis, MO) and maintained at 2% oxygen and 5% CO2 in a humidified chamber (Billups-Rothenberg, Del Mar, CA) for 48 hours. Cells were plated at 8.3 x 10^3/ml (MethoCult M3534 Stem Cell Technologies, Vancouver, Canada) and maintained in 2% oxygen and 5% CO2. After seven days, colonies were counted.
**Figure S1. Proliferation of PR progenitors.** (A) Cell counts and (B) cell cycle analysis by BrdU / 7-AAD of myeloid progenitors derived from WT, PR$^{WT}$ or PR$^{2VR}$ preleukemic mice incubated and with G-CSF and SCF demonstrating no major differences in cell proliferation between PR$^{WT}$ or PR$^{2VR}$.

**Figure S2. In vitro differentiation of PR progenitors.** (A) Flow cytometry of myeloid progenitors from WT, PR$^{WT}$ or PR$^{2VR}$ preleukemic mice in G-CSF and SCF at 2, 4, and 6 days after plating demonstrating increase in Gr-1, CD11b staining and loss of CD117 indicating differentiation of progenitors *in vitro*. No major differences are observed between PR$^{WT}$ and PR$^{2VR}$.

**Figure S3. ATRA induced differentiation of PR tumors.** Loss of colony forming units in PR$^{WT}$ and PR$^{2VR}$ tumors following exposure to 1μM ATRA compared to wild type progenitors.
A

**Figure S1**
Figure S2
Figure S3