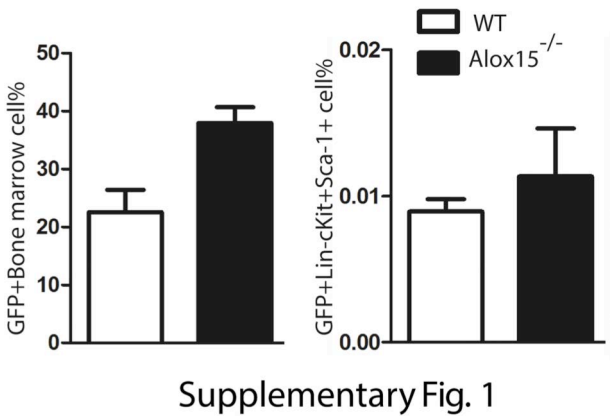
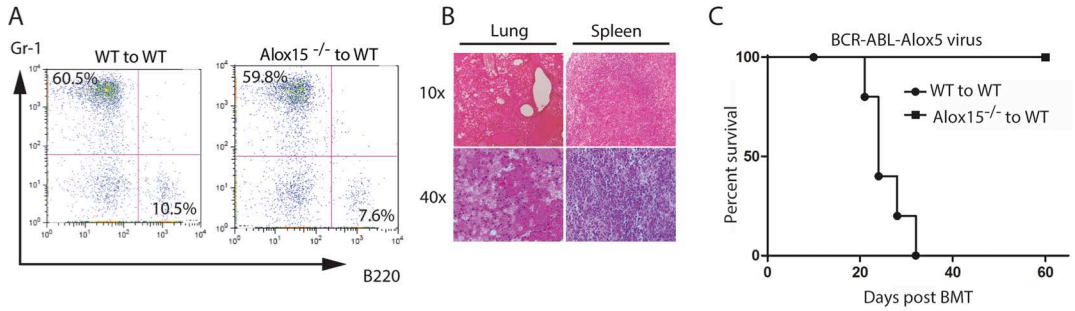
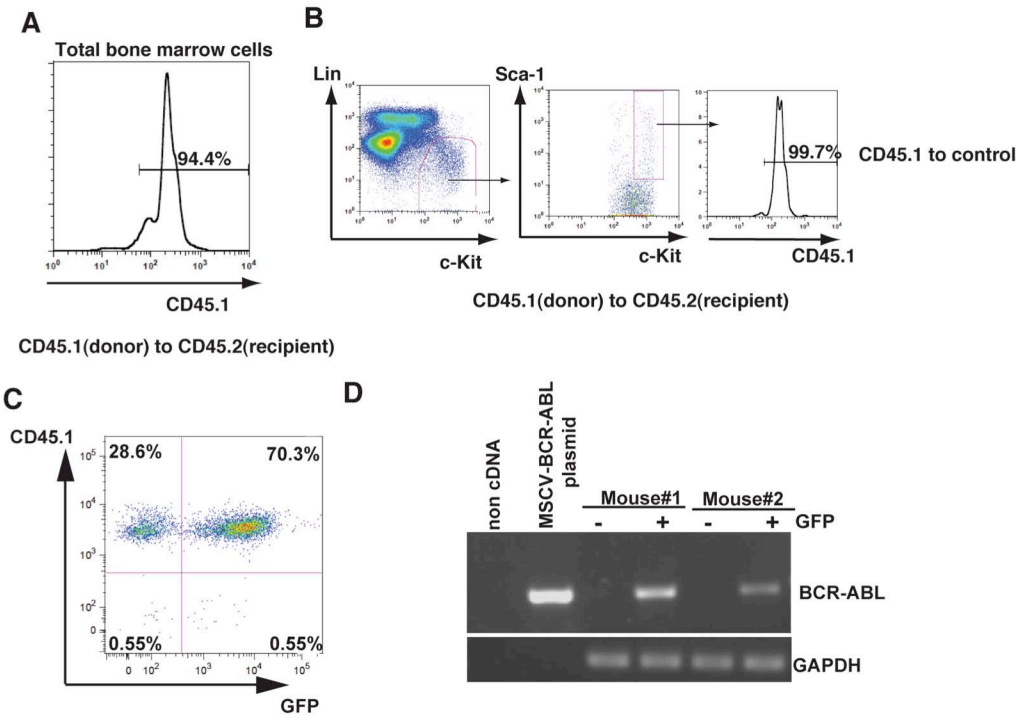


Supplemental Figure 1. Retroviral transduction efficiency of WT and *Alox15*$^{-/-}$ BM cells and LSK cells. The BM cells from WT and *Alox15*$^{-/-}$ mice were prestimulated with IL-3, IL-6, and SCF, transduced with a MSCV-based retrovirus expressing GFP and cultured for 48h. Viable WT or *Alox15*$^{-/-}$ GFP^{+} BM cells (left panel) and GFP^{+} LSK (Lin^{-} Sca-1^{+}c-Kit^{+}) cells (right panel) were compared by FACS.



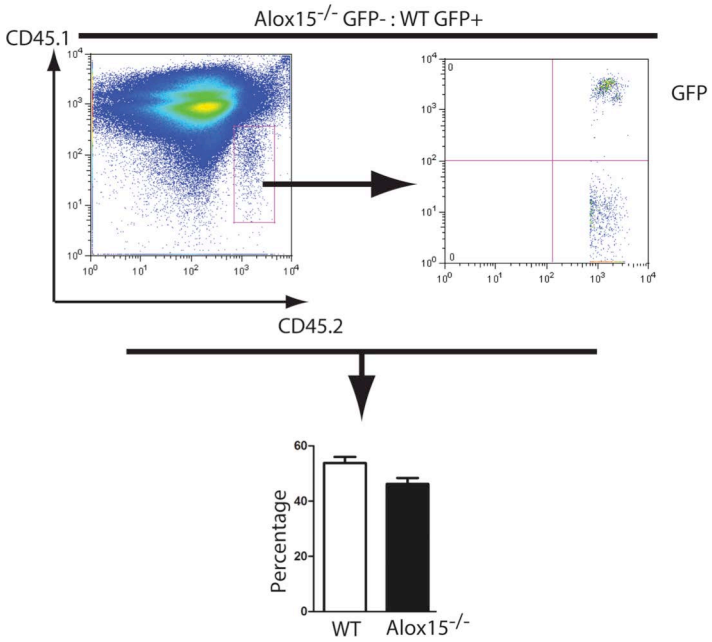
Supplementary Fig. 2

Supplemental Figure 2. (A) Alox15 transgene rescues the defective CML phenotype. *BCR-ABL* and *Alox15* were co-expressed in *Alox15*$^{-/-}$ BM cells by retroviral transduction, followed by transplantation of the transduced cells into WT recipient mice. FACS analysis showed similar percentages of Gr-1^{+} cells in PB of both groups of CML mice. (B) Over-expression of *Alox15* rescues the defective CML phenotype. *BCR-ABL* and *Alox15* were co-expressed in *Alox15*$^{-/-}$ BM cells by retroviral transduction, followed by transplantation of the transduced cells into WT recipient mice. Photomicrographs of hematoxylin and eosin-stained lung and spleen sections from CML mice receiving *BCR-ABL-Alox15* transduced *Alox15*$^{-/-}$ BM cells. (C) *Alox5* does not rescue defective CML phenotype caused by *Alox15* deficiency. Kaplan-Meier survival curves for recipients of *BCR-ABL-IRES-Alox5-pMSCV*-transduced BM cells from WT (n =5) or *Alox15*$^{-/-}$ (n=5) donor mice.



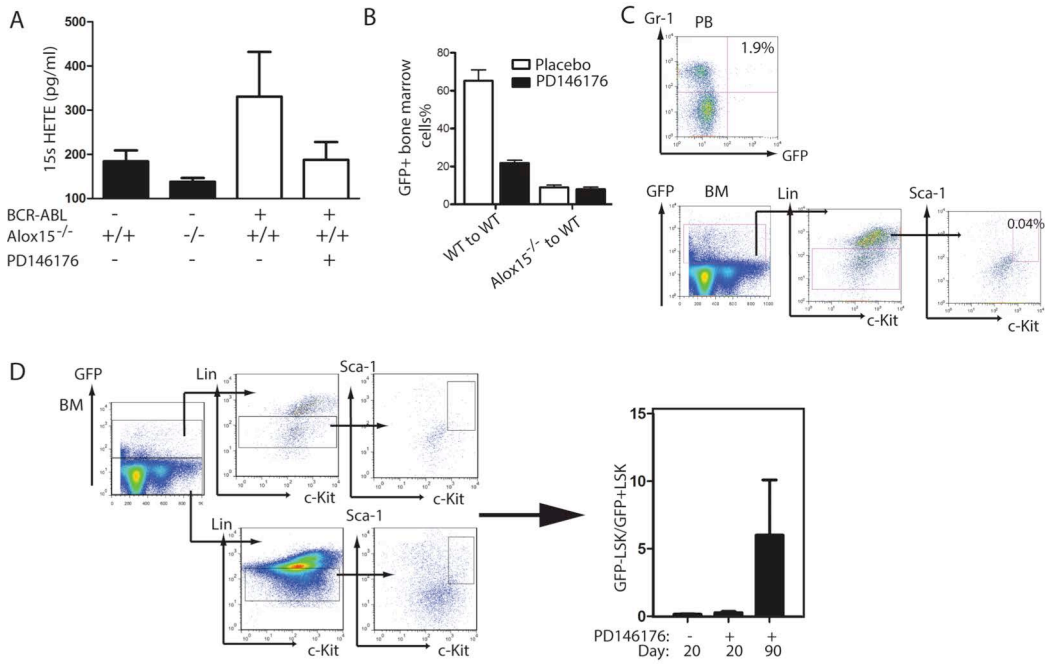
Supplementary Fig. 3

Supplemental Figure 3. Total BM and LSK cells in lethally-irradiated recipient mice are derived from donor but not recipient BM cells. $5x10^6$ CD45.1 donor BM cells were isolated and transplanted into lethally irradiated recipient mice (CD45.2). At day 14 after transplantation, FACS analysis showed the percentages of donor-derived $CD45.1^+$ BM cells (A) and $CD45.1^+$ LSK ($Lin^-Sca\text{-}1^+c\text{-}Kit^+$) (B) in BM of recipient mice. (C) CD45.1 donor BM cells were transduced by BCR-ABL retrovirus and then injected into CD45.2 recipient mice that were lethally irradiated. At day 14 after transplantation, FACS analysis showed the percentages of donor-derived $CD45.1^+$ BM cells. (D) Blood cells from CML mice were sorted into GFP^+ and GFP^- cells by FACS, and Total RNA was isolated, and real-time PCR was performed to detect the BCR-ABL transcripts.



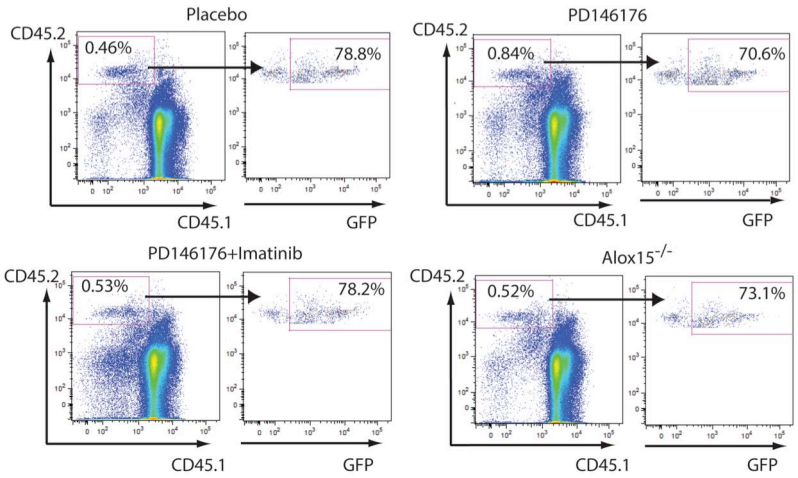
Supplementary Fig. 4

Supplemental Figure 4. *Alox15*$^{-/-}$ BM cells did not have a homing defect. BM cells ($5x10^6$) from GFP mice (CD45.2) and *Alox15*$^{-/-}$ mice (CD45.2) were 1:1 mixed, and then transferred by tail vein injection into the same WT recipient mouse (CD45.1). 3h after transplantation, by FACS analysis, CD45.2$^+$ BM cells, representing the donor cells, were identified, and then analyzed for the percentages of the GFP$^+$ and GFP$^-$ populations.



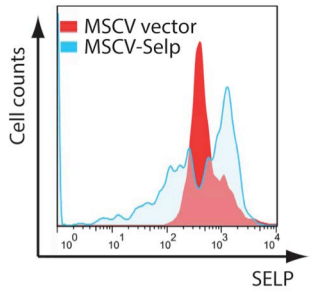
Supplementary Fig. 5

Supplemental Figure 5. (A) PD146176 treatment reduces the plasma level of 15s HETE in CML mice. CML mice were treated with PD146176 for 8 days, beginning at 8 days after induction of CML. The plasma levels of 15s HETE were detected by ELISA (Cayman Chemical Company). Mean value (± s.d.) was shown for each group. WT and *Alox15*$^{-/-}$ mice were used as controls. (B) PD146176 treatment inhibits *Alox15* function in CML mice. WT or *Alox15*$^{-/-}$ donor BM cells were transduced with *BCR-ABL* to induce CML. 8 days after CML induction, the mice were treated with or without PD146176 for one week. PD146176 significantly inhibited WT *BCR-ABL*-expressing BM cells (GFP^{+}) but failed to further inhibit *Alox15*$^{-/-}$ *BCR-ABL*-expressing BM cells. (C) Long-term effect of *Alox15* inhibition on LSCs and CML development. CML mice were treated with PD146176 until 90 days after CML induction, and blood and BM cells were isolated. (D) Long-term effect of *Alox15* inhibition on LSCs and HSCs. CML mice were treated with PD146176 until 90 days after CML induction, and BM cells were isolated from the treated CML mice for FACS analysis of HSCs and LSCs in BM.



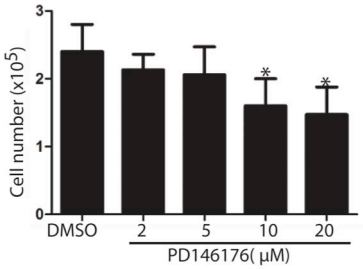
Supplementary Fig. 6

Supplemental Figure 6. Alox15 inhibition does not affect the homing/invasion of CML cells in CML mouse model. GFP^+ BM cells from CML mice (CD45.2) treated with PD146176 alone or PD146176 combined with imatinib were isolated and then transferred by tail vein injection into the same WT recipient mouse (CD45.1). 3h after transplantation, by FACS analysis, $CD45.2^+$ BM cells, representing the donor cells, were identified, and then analyzed for the percentages of the GFP^+ and GFP^- populations.



Supplementary Fig. 7

Supplemental Figure 7. Over-expression of SELP in blood cells. WT BM cells were transduced with an empty GFP-expressing retrovirus and *MSCV-Selp* over-expressed retrovirus, followed by transplantation into recipient mice. The expression of SELP was determined by FACS at day 30 post transplantation.



Supplementary Fig. 8

Supplemental Figure 8. PD146176 inhibits the proliferation of HL60 cells. HL60 cells were treated with DMSO or PD146176 (2, 5, 10, 15, and 20μM, respectively) for 48h and live cells were determined by trypan blue staining.