Supplemental Figure Legends

Supplemental Figure 1. Survival curve demonstrating that co-culture on VeraVec results in more aggressive leukemic cells. 50,000 leukemic cells cultured without feeder layers in 10% serum and co-cultured with VeraVec in serum free + 50 ng/mL of sKitL were injected into sublethally irradiated mice (650 Rads) and after 20 days, all mice transplanted with leukemic cells co-cultured on VeraVec were moribund and sacrificed. The bone marrow (BM) and spleen were collected and analyzed by flow cytometry (n=10 per cohort, 2 independent experiments from 2 different clones used for Figure 1). The remaining mice that were either transplanted or not transplanted with leukemic cells cultured in 10% serum were allowed to survive to generate the survival curve. Significance of Survival Curve was determined by Log Rank Test (*P<0.05. **P<0.001).

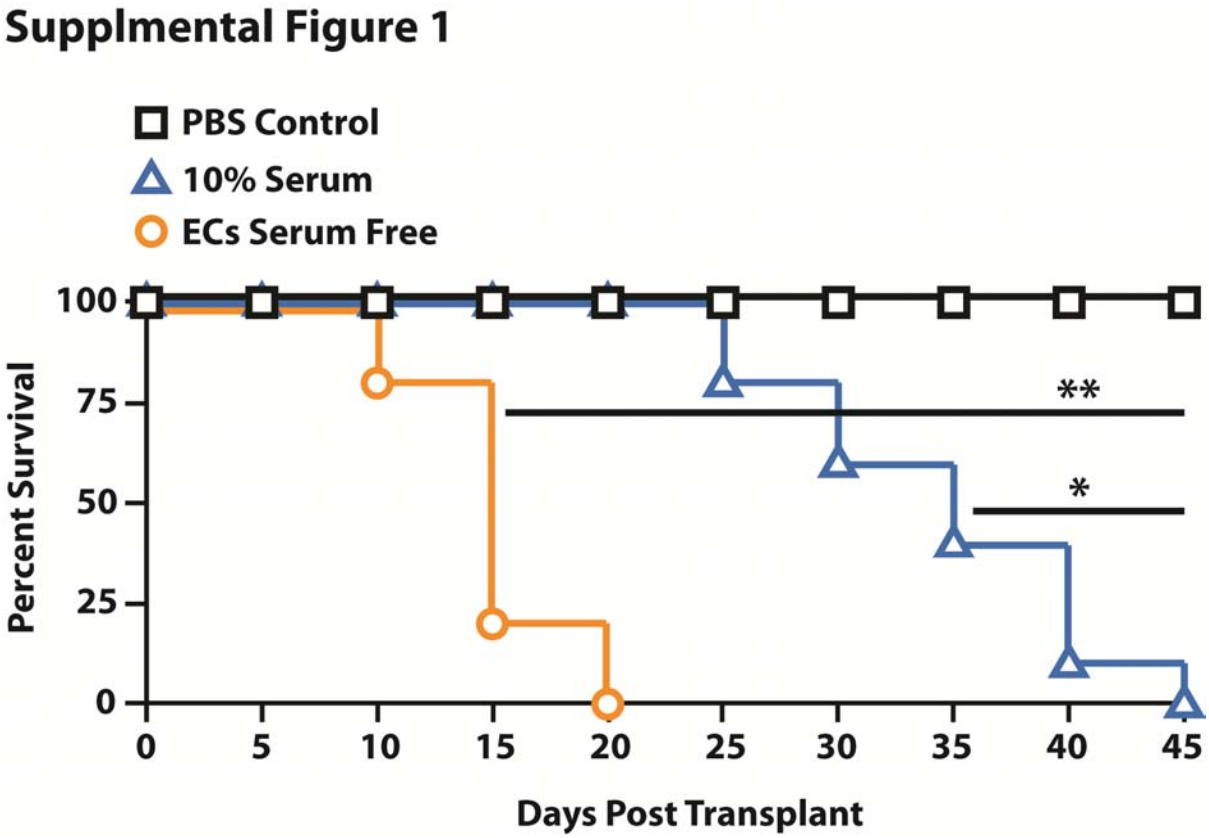
Supplemental Figure 2. VEGF-A does not directly affect the expansion of MLL-AF9 LICs. MLL-AF9 GFP^+ clones were cultured in 10% serum supplemented with either 50 ng/mL sKitL or with 50 ng/mL sKitL plus 20 ng/mL VEGF-A for 14 days (all culture conditions were without the support of VeraVec). The addition of VEGF-A to LICs did not increase the cumulative expansion of LICs generated from any clones.

Supplemental Figure 3. Schematic for *in vivo* experiments. A) On day 0, animals were sublethally irradiated (650 Rads) and were transplanted with 5×10^5 GFP^+ AML cells that were cultured in 10% serum supplemented with 50 ng/mL sKitL for 7 days. On day 15 post transplant, 5 mice from each cohort were sacrificed and the BM and spleen were analyzed for GFP^+ AML leukemia. The remaining 15 mice were allowed to live to

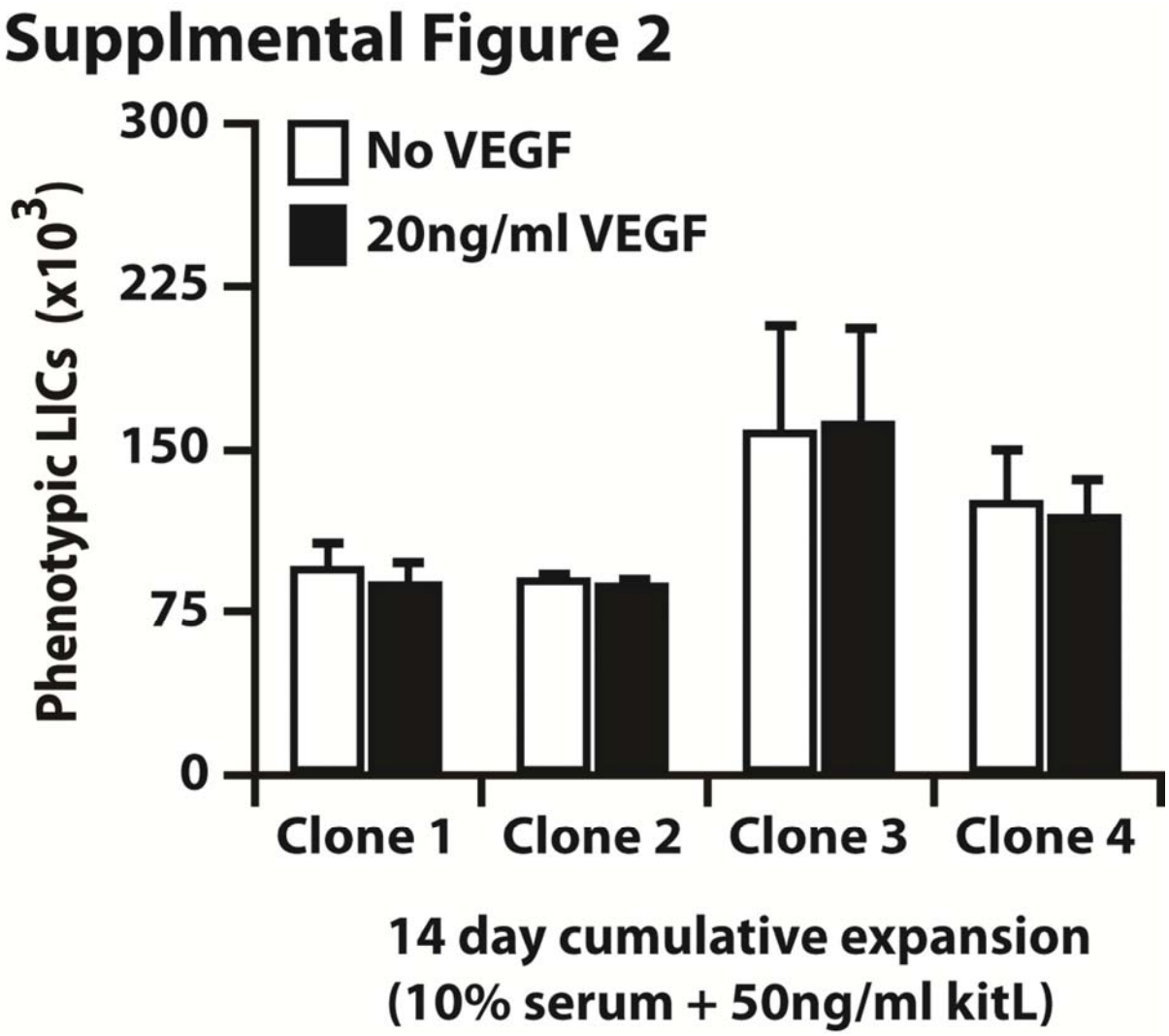
generate survival curves. Three individual MLL-AF9 clones were used in 3 independent experiments. B) VEGF-A, αVEGFR2, and Ara-C dosing schedule.

Supplemental Figure 4. MLL-AF9 LICs do not express VEGF receptors. Lineage$^-$ cKit$^+$CD16/32$^+$CD34$^+$ GMPs were isolated from mice and MLL-AF9 GFP$^+$ transduced GMPs were generated (5 clones). MLL-AF9 GFP$^+$ cell lines were transplanted into sublethally irradiated mice (650 Rads; 1 cell line/5 mice). **A-B)** Mice were allowed to generate GFP$^+$ leukemia as demarcated by peripheral blood analysis (60-80% GFP$^+$). Bone marrow was isolated and underwent flow cytometric analysis. Lineage$^-$ CD16/32$^+$CD34$^+$ cells were divided into cKit$^+$ and cKit$^+$GFP$^+$ groups and were analyzed for expression of VEGFR1 and VEGFR2 and each receptor from each fraction was compared to IgG controls. **A)** The cKit$^+$GFP$^-$ fraction did not express VEGFR2, but did express high levels of VEGFR1 when compared with cKit$^-$GFP$^-$. **B)** The cKit$^+$GFP$^+$ fraction did not express either VEGFR1 or VEGFR2. **C)** Representative histograms and dot plots. All data represents mean $\pm$ s.d. (***P<0.0001, n.s.=not significant).

Supplmental Figure 1

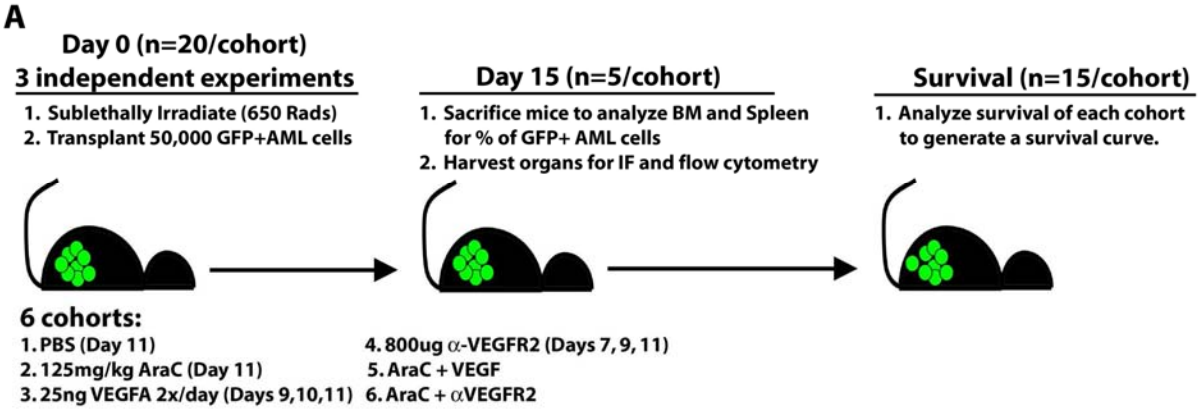


Supplmental Figure 2



Supplmental Figure 3

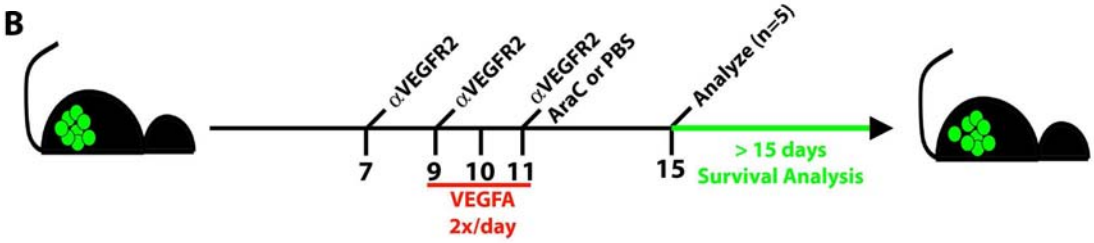
A



6 cohorts:

1. PBS (Day 11)
2. 125mg/kg AraC (Day 11)
3. 25ng VEGFA 2x/day (Days 9,10,11)
4. 800ug α-VEGFR2 (Days 7, 9, 11)
5. AraC + VEGF
6. AraC + αVEGFR2

B



Supplemental Figure 4