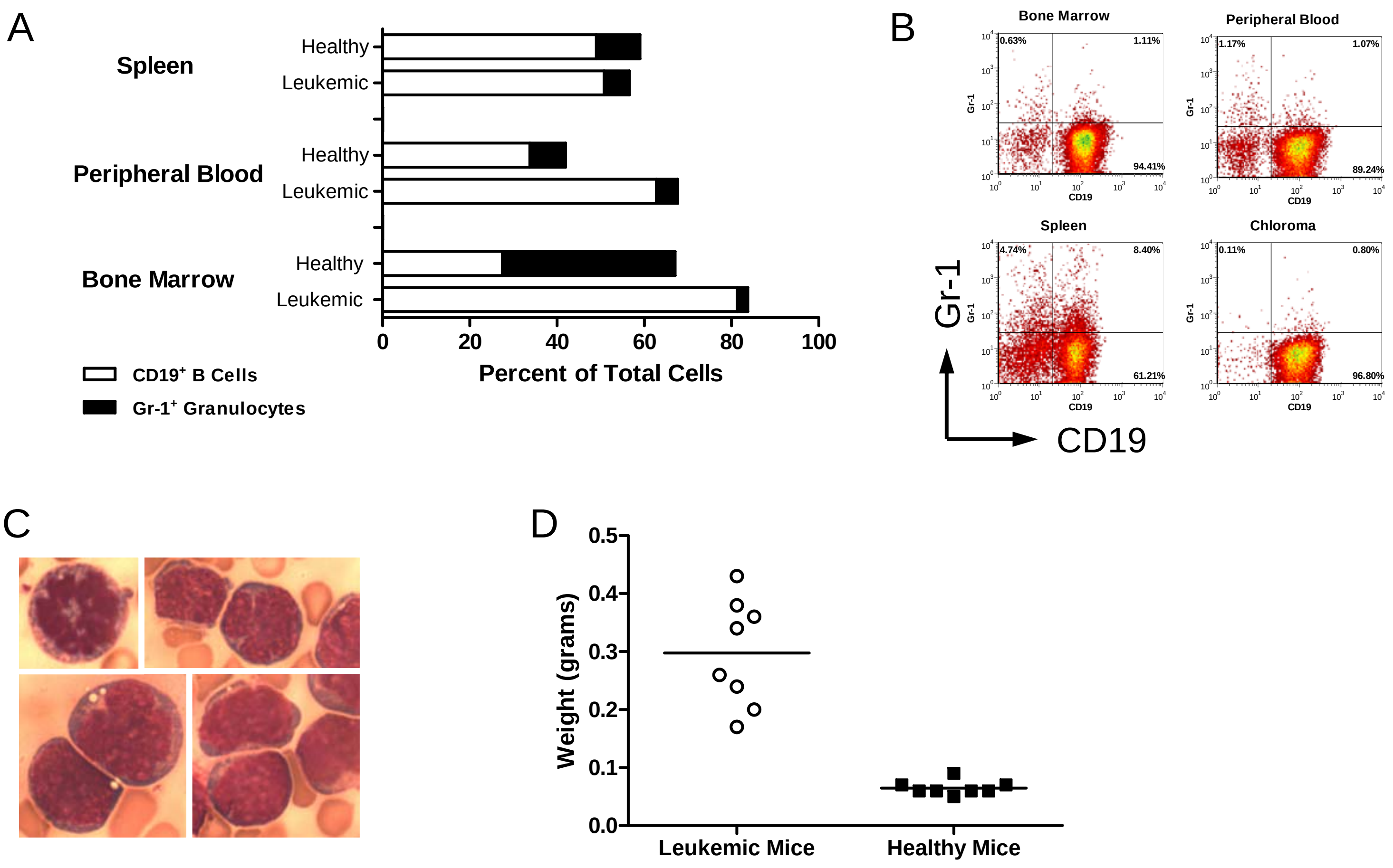
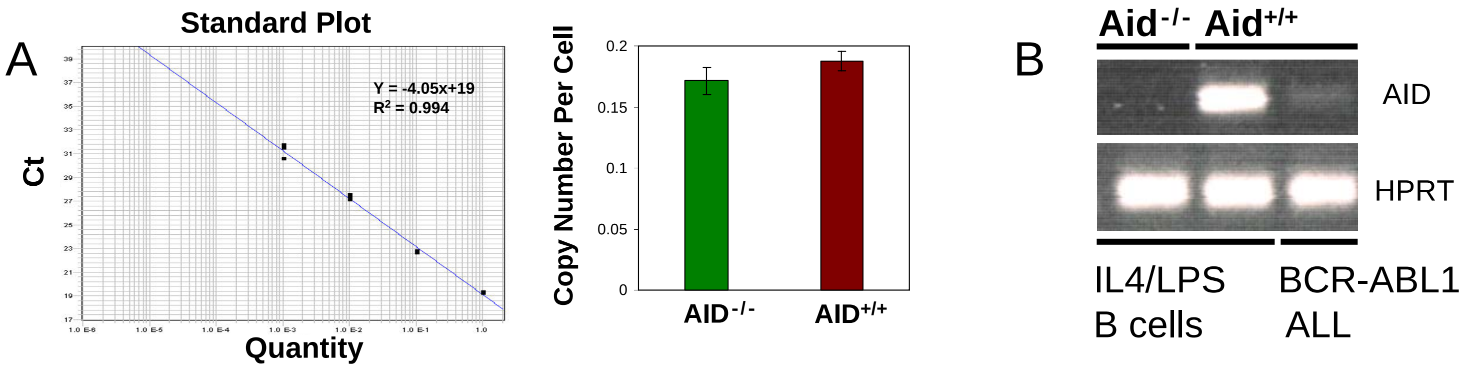
Figure S1: *Disease burden in leukemic mice*

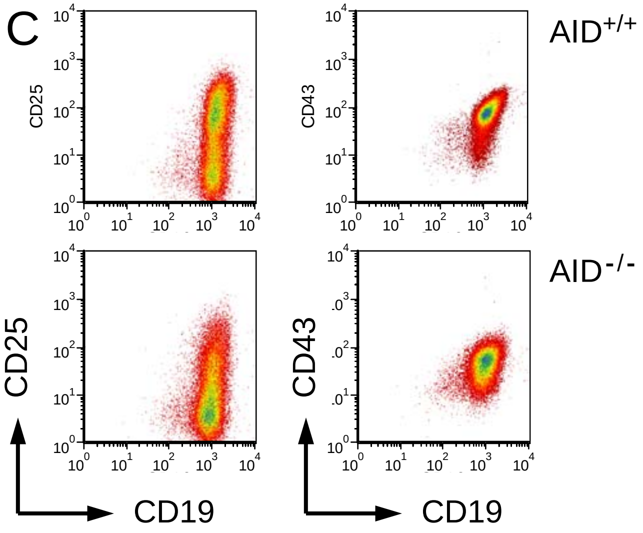


Legend to Figure S1.

(A) White blood cell differential counts in the spleen, peripheral blood (PBL), and bone marrow (BM) as determined by flow cytometry in mice developing leukemia. Gr-1 is a murine myeloid marker and CD19 represents the B cell population. Data is compiled from 8 leukemic mice and 8 healthy mice. (B) Representative flow cytometry data of a mouse with leukemia. Several mice developed solid masses of leukemia cells labeled here as “chloroma” in the above figure. (C) Peripheral blood smear of a diseased mouse demonstrating the presence of leukemic blasts, some of which were undergoing mitosis (upper left hand photo). (D) Spleen weight in mice developing leukemia compared to healthy mice.

Figure S2: *Transformation characteristics of AID$^{+/+}$ and AID$^{-/-}$ BCR-ABL1 ALL*





Legend to Figure S2.

(A) Quantitative real time PCR of the *BCR-ABL1* gene in AID$^{-/-}$ and AID$^{+/+}$ bone marrow transplanted into lethally irradiated recipients (see Figure 1). BM185 cells were used as a standard. BM185 is a *BCR-ABL1* transformed pre-B cell clone that has one copy of the oncogene per cell as determined by Southern blot analysis. (B) RT-PCR of AID mRNA expression in BCR-ABL1-transformed ALL cells from AID$^{-/-}$ and AID+/+ mice is shown. Activated mature B cells (IL4, LPS) are used as positive control and HPRT is used as reference gene for RT-PCR analysis. (C) Flow cytometry was performed to compare the phenotype and differentiation stage of full-blown leukemia from AID$^{+/+}$ and AID$^{-/-}$ animals. Leukemia cells were stained with antibodies against the pan-B cell antigen CD19, the pre-B cell antigen CD25 and CD43, which is expressed on both pro- and pre-BI cells.

Figure S3. *Mechanisms of Imatinib resistance.*

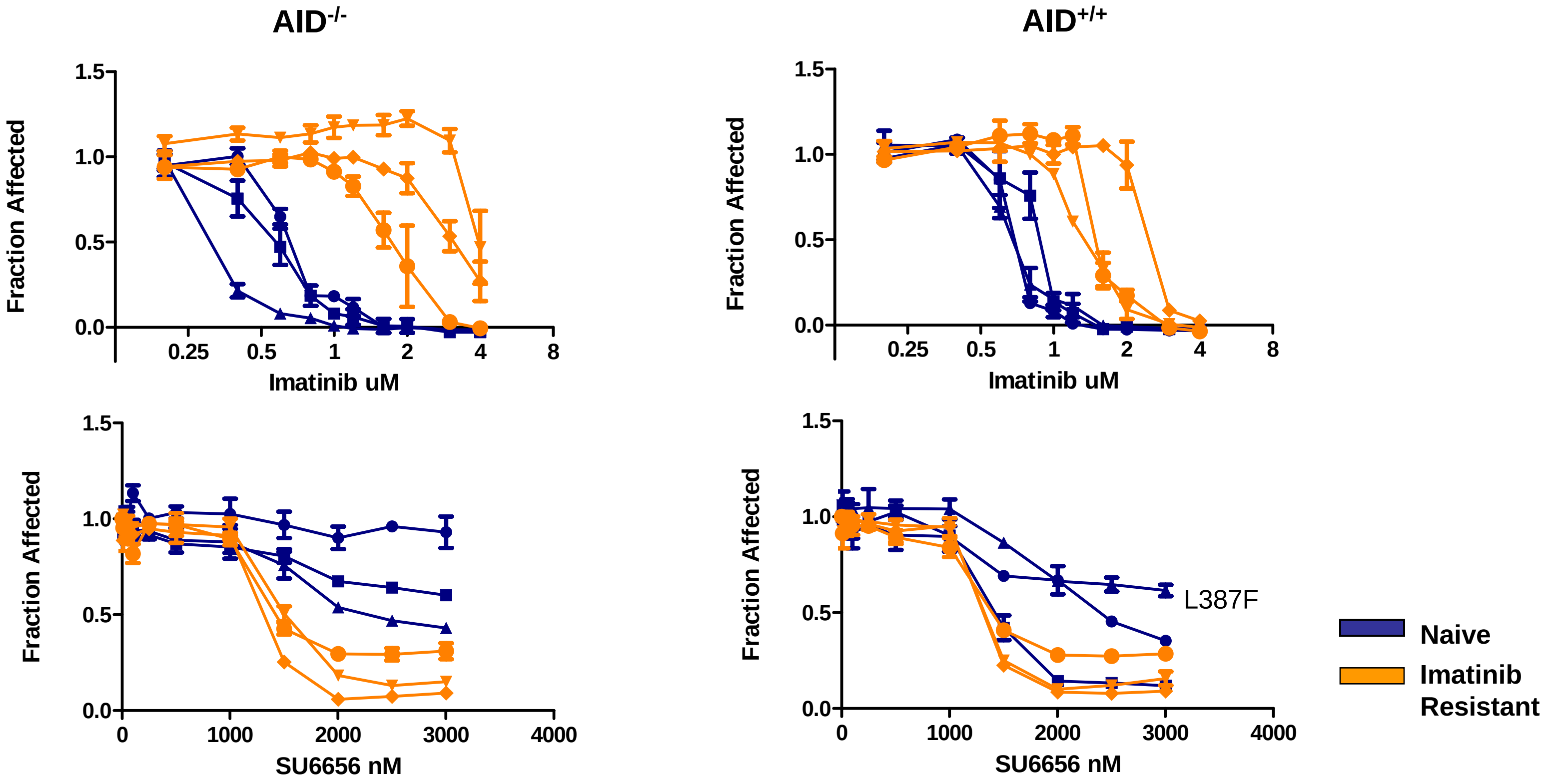
A.

Kinase Domain Sequencing of Imatinib Resistant Leukemia

Cohort	N	Mutation	Clones with Mutation	Imatinib Resistance*
AID $^{-/-}$	3			
K3.3		None	0/11	NA
K5.3		None	0/11	NA
K7.3		V280G	10/11	No
AID$^{+/+}$	3			
W7.3		None	0/11	NA
W10.3		None	0/11	NA
W11.3		L387F	12/14	Yes

*Soverini et al., 2006.

B.



Legend to Figure S3. *Mechanisms of Imatinib resistance.*

A. Kinase domain sequencing of the *BCR-ABL1* oncogene. Three AID$^{-/-}$ and three AID$^{+/+}$ samples were grown in increasing concentrations of Imatinib every four to seven days, beginning with 0.05 µmol/l and ending with 1µmol/l. DNA was extracted from Imatinib resistant cells, and the kinase domain was amplified, cloned and sequenced as described in Materials and Methods. B. Sensitivity of Imatinib resistant leukemia to Src inhibition. Imatinib resistant cells were generated as described in A. Imatinib resistant and Imatinib naïve cells were then plated and treated with increasing concentrations of either Imatinib or SU6656 as indicated. After 72 hours of incubation, proliferation was measured using a standard MTT assay. The AID$^{+/+}$ clone with a kinase domain mutation is indicated (L387F). Data is a representative example of results seen in three repeat experiments.

Table S1. Genes Amplified and Deleted in AID$^{-/-}$ and AID$^{+/+}$ leukemia

Amplified						Deleted					
AID$^{-/-}$ Mouse K3	**AID$^{-/-}$ Mouse K5**	**AID$^{-/-}$ Mouse K7**	**AID$^{+/+}$ Mouse W7**	**AID$^{+/+}$ Mouse W10**	**AID$^{+/+}$ Mouse W11**	**AID$^{-/-}$ Mouse K3**	**AID$^{-/-}$ Mouse K5**	**AID$^{-/-}$ Mouse K7**	**AID$^{+/+}$ Mouse W7**	**AID$^{+/+}$ Mouse W10**	**AID$^{+/+}$ Mouse W11**
Adam6	Arid5b	Adam6	Apol7c	Apol7c	Apol7c	Alox5	Cass4	Alox5	Adam6	Adam6	Adam6
Btbd9	Btbd9	Alk	Apol10a	Apol10a	Apol10a	Cass4	Crxos1	Cass4	Anln,	Anln,	Anln,
Dnahc8	Dnahc8	Btbd9	Btbd9	Btbd9	Btbd9	Crxos1	Gcnt7	Crxos1	Bbs9	Bbs9	Bbs9
Glo1	Fst	Bzrap1	Chia	Chia	Btla	Gcnt7	H1foo	Gcnt7	Cass4	Cass4	Cass4
Glp1r	Glo1	Ccdc124	Chi3l3	Chi3l3	Chia	Luzp1	Luzp1	Luzp1	Ccne2	Ccne2	Ccne2
Gm711	Glp1r	Dnahc8	Chi3l4	Chi3l4	Chi3l3	Pla2g2e	Pla2g2e	Pla2g2e	Cd244	Ctnnd2	Cd244
Matn3	Gm711	Fst	Dap3	Dnahc8	Chi3l4	V1rf2	V1rf2	V1rf2	Ctnnd2	Cyp2b9	Ctnnd2
Msh3	Matn3	Glo1	Dnahc8	Glo1	Dnahc8	V1rf4	V1rf4	V1rf4	Cyp2b9	Cyp2b13	Cyp2b9
Mup1	Msh3	Glp1r	Glo1	Iltifb	Fst	Tcfe3	Tcfe3		Cyp2b13	Ddx3y	Cyp2b13
Mup2	Mup1	Gm711	Irx5	Matn3	Glo1				Ddx3y	Ebag9	Ddx3y
Mup5	Mup2	Matn3	Kcnj11	Mup1	Iltifb				Ebag9	Eif2s3y	Ebag9
Naip1	Mup5	Mpo	Klf17	Mup2	Matn3				Eif2s3y	Gcnt7	Eif2s3y
Obox1	Naip1	Msh3	Klhl1	Mup4	Mup1				Gcnt7	H2al2y	Gcnt7
Obox3	Obox1	Mup1	Matn3	Mup5	Mup2				H2al2y	Ints8	H2al2y
Obox5	Obox3	Mup2	Msto1	Nrxn3	Mup4				Ints8	Jarid1d	Ints8
Rexo4	Obox5	Mup4	Mup1	Olfr1040	Mup5				Itln1	Pgcp	Itln1
Setx	Osbpl3	Mup5	Mup2	Osbpl3	Nrxn3				Jarid1d	rp9	Jarid1d
Surf4	Rexo4	Naip1	Mup5	Scoc	Olfr1040				Pgcp	Sntg1	Pgcp
V1rd14	Setx	Obox1	Nomo1	Serpina1a	Osbpl3				rp9	Sry	Ptprn2
V1rd21	Sox6	Obox3	Nrxn3	Serpina1c	Serpina1a				Tmem181	Trpm8	rp9
	Surf4	Obox5	Olfr1040	Serpina1e	Serpina1c				Trpm8	Ube1y1	Tmem181
chr12 (entire)	V1rd14	Osbpl3	Osbpl3	Sirpb1	Serpina1e				Tulp4	Ugt1a1	Trpm8
	V1rd21	Rexo4	Rap1gap	Skint6	Sirpb1				Sry	Ugt1a2	Tulp4
		Setx	Scoc	Slc9a10	Skint6				Sytl3	Ugt1a5	Sntg1
		Sox6	Serpina1a	Sox6	Slc9a10				Ube1y1	Ugt1a6a	Sry
		Surf4	Serpina1c	Stfa1	Sox6				Ugt1a1	Ugt1a6b	Sytl3
		V1rd14	Serpina1e		Stfa1				Ugt1a2	Ugt1a7c	Ube1y1
		V1rd21	Sirpb1	chr X (entire)					Ugt1a5	Ugt1a9	Ugt1a1
			Skint6		chr X (entire)				Ugt1a6a	Ugt1a10	Ugt1a2
			Slc9a10						Ugt1a6b	Uty	Ugt1a5
			Sox6						Ugt1a7c	Vmn2r121	Ugt1a6a
			Stfa1						Ugt1a9	Zfy1	Ugt1a6b
			Zscan4f						Ugt1a10	Zfy2	Ugt1a7c
									Usp9y		Ugt1a9
			chr18 (entire)						Uty		Ugt1a10
			chr X (entire)						Vmn2r121		Usp9y
									Zfy1		Uty
									Zfy2		Vmn2r121
											Zfy1
											Zfy2

Genes listed in alphabetical order.

Aberration detection method 2 (ADM-2) with centralization, fuzzy correction, and default filters was used to define aberrant intervals with DNA Analytics 4.0 software.

Table S2. Genes differentially expressed in AID$^{-/-}$ vs. AID$^{+/+}$ leukemia

Probe Set ID	Gene Title	Gene Symbol	Fold Change	F ratio*	p-value*
Upregulated in AID$^{-/-}$					
1459854_s_at	dynein light chain Tctex-type 3	Dynlt3	83.06	4781.29	2.62E-07
1452077_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked	Ddx3y	49.13	4228.9	3.35E-07
1426523_a_at	glucosamine-6-phosphate deaminase 2	Gnpda2	45.13	3779.02	4.19E-07
1424903_at	jumonji, AT rich interactive domain 1D (Rbp2 like)	Jarid1d	33.87	3402.59	5.17E-07
1426535_at	KTEL (Lys-Tyr-Glu-Leu) containing 1	Ktelc1	21.88	3019.42	6.57E-07
1420614_at	dynein light chain Tctex-type 3	Dynlt3	40.46	2927.37	6.99E-07
1459843_s_at	MAD homolog 1 (Drosophila)	Smad1	59.55	2742.57	7.96E-07
1446627_at	---	---	5.76	2575.49	9.02E-07
1426438_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked	Ddx3y	95.19	2445.98	1.00E-06
1450021_at	ubiquilin 2	Ubqln2	174.04	2147	1.30E-06
1450959_at	RIKEN cDNA D930014E17 gene	D930014E17Rik	20.83	2025.9	1.46E-06
1449929_at	dynein light chain Tctex-type 3	Dynlt3	79.13	1942.43	1.58E-06
1434131_at	RUN and FYVE domain containing 1	Rufy1	12.9	1881.39	1.69E-06
1421947_at	guanine nucleotide binding protein (G protein), gamma 12	Gng12	18.14	1864.4	1.72E-06
1434665_at	aspartylglucosaminidase	Aga	2.63	1789.5	1.87E-06
1426439_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked	Ddx3y	28.38	1663.99	2.16E-06
1437002_at	family with sequence similarity 73, member A	Fam73a	5.07	1647.13	2.20E-06
1448892_at	dedicator of cytokinesis 7	Dock7	38.62	1566.79	2.43E-06
1434857_at	RIKEN cDNA A230106D06 gene	A230106D06Rik	17.31	1523.74	2.57E-06
1440972_at	nuclear receptor-binding SET-domain protein 1	Nsd1	1.7	1452.49	2.83E-06
1448844_at	cytochrome b5 type B	Cyb5b	2.1	1084.55	5.07E-06
1451721_a_at	histocompatibility 2, class II antigen A, beta 1 /// response to metastatic canc	H2-Ab1 /// Rmcs2 /// Rmcs5	6.62	1034.43	5.57E-06
1449124_at	ral guanine nucleotide dissociation stimulator,-like 1	Rgl1	2.65	1031.34	5.60E-06
1453071_s_at	KDEL (Lys-Asp-Glu-Leu) containing 2	Kdelc2	12.42	1011.99	5.82E-06
1416554_at	similar to Pdlim1 protein /// PDZ and LIM domain 1 (elfin)	LOC100048338 /// Pdlim1	21.13	1010.17	5.84E-06
1458585_at	---	---	5.57	1002.48	5.93E-06
1415831_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 2	Psmd2	1.21	1002.26	5.93E-06
1426598_at	ubiquitously transcribed tetratricopeptide repeat gene, Y chromosome	Uty	11.95	958.745	6.48E-06
1428695_at	short chain dehydrogenase/reductase family 39U, member 1	Sdr39u1	3.08	938.464	6.76E-06
1429519_at	fucose-1-phosphate guanylyltransferase	Fpgt	26.53	930.051	6.89E-06
1438504_x_at	Transmembrane 7 superfamily member 3 (Tm7sf3), mRNA	Tm7sf3	13.47	929.388	6.90E-06
1433695_at	cannabinoid receptor interacting protein 1	Cnrip1	21.69	926.451	6.94E-06
1449870_a_at	ATPase, H+ transporting, lysosomal V0 subunit A2	Atp6v0a2	1.51	900.951	7.34E-06
1440263_at	neural regeneration protein	Nrp	1.55	863.884	7.98E-06
1428972_at	Tctex1 domain containing 2	Tctex1d2	24.84	804.155	9.20E-06
1460359_at	armadillo repeat containing, X-linked 3 /// hypothetical protein LOC100044266	Armcx3 /// LOC100044266	12.9	792.053	9.48E-06
1416020_a_at	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit c (subunit 9),	Atp5g1 /// ENSMUSG00000058357	1.5	754.148	1.05E-05
1428458_at	processing of precursor 1, ribonuclease P/MRP family, (S. cerevisiae)	Pop1	2.34	744.595	1.07E-05
1416007_at	special AT-rich sequence binding protein 1	Satb1	21.3	737.342	1.09E-05
1436350_at	family with sequence similarity 171, member B	Fam171b	1.8	726.688	1.13E-05
1458719_at	---	---	1.98	722.741	1.14E-05
1456395_at	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha	Ppargc1a	6	721.836	1.14E-05
1453287_at	ankyrin repeat domain 33B	Ankrd33b	13.32	721.296	1.14E-05
1434138_at	prune homolog (Drosophila)	Prune	1.46	714.911	1.16E-05
1436910_at	RAS protein activator like 2	Rasal2	12.07	696.401	1.23E-05
1455213_at	RIKEN cDNA 4930488E11 gene /// thymosin beta-like	4930488E11Rik /// LOC100034363	10.32	692.862	1.24E-05
1458274_at	zinc finger protein 69	Zfp69	2.34	676.526	1.30E-05
1417886_at	RIKEN cDNA 1810009A15 gene /// hypothetical protein LOC100048454	1810009A15Rik /// LOC100048454	1.7	668.652	1.33E-05
1455719_at	tubulin, beta 5	Tubb5	3.77	666.686	1.34E-05
1438463_x_at	zinc finger, DHHC domain containing 6	Zdhhc6	1.16	663.329	1.35E-05
1447934_at	RIKEN cDNA 9630033F20 gene /// similar to RIKEN cDNA 9630033F20 gene	9630033F20Rik /// LOC677429	2.29	656.517	1.38E-05
1426524_at	glucosamine-6-phosphate deaminase 2	Gnpda2	24.14	642.712	1.44E-05
1428331_at	RIKEN cDNA 2210016F16 gene	2210016F16Rik	11.78	632.922	1.48E-05

1457259_at	similar to sorting nexin 6	LOC100047864	2.12	627.753	1.51E-05
1441071_at	potassium voltage-gated channel, subfamily Q, member 5	Kcnq5	8.16	627.338	1.51E-05
1418394_a_at	CD97 antigen	Cd97	18.26	623.958	1.52E-05
1437303_at	interleukin 6 signal transducer	Il6st	6.77	591.027	1.70E-05
1429399_at	ring finger protein 125	Rnf125	33.07	589.892	1.70E-05
1415698_at	golgi membrane protein 1	Golm1	11.05	588.225	1.71E-05
1416782_s_at	PRA1 domain family 2	Praf2	5.87	586.751	1.72E-05
1459733_at	---	---	2.94	566.196	1.85E-05
Downregulated in AID$^{-/-}$					
1427262_at	inactive X specific transcripts	Xist	-411.08	10855.5	5.09E-08
1441264_x_at	RIKEN cDNA A930005H10 gene	A930005H10Rik	-1.71	4552.33	2.89E-07
1441885_s_at	---	---	-11	2495.52	9.61E-07
1452426_x_at	---	---	-36.15	2358.79	1.08E-06
1452483_a_at	CD44 antigen	Cd44	-9.02	1949.49	1.57E-06
1437538_at	small nucleolar RNA host gene (non-protein coding) 7	Snhg7	-2.09	1847.07	1.75E-06
1454959_s_at	guanine nucleotide binding protein (G protein), alpha inhibiting 1	Gnai1	-94.14	1735.76	1.98E-06
1439847_s_at	Kruppel-like factor 12	Klf12	-11.63	1710.17	2.04E-06
1439055_at	predicted gene, OTTMUSG00000025408	OTTMUSG00000025408	-6.87	1640.2	2.22E-06
1440870_at	PR domain containing 16	Prdm16	-16.95	1385.96	3.11E-06
1439196_at	hook homolog 3 (Drosophila)	Hook3	-1.19	1337.59	3.34E-06
1418504_at	heat shock protein 9	Hspa9	-1.55	1232.51	3.93E-06
1452452_at	---	---	-1.72	1149.14	4.52E-06
1435789_x_at	---	---	-1.88	1115.44	4.79E-06
1425493_at	bone morphogenetic protein receptor, type 1A	Bmpr1a	-14.2	1080.53	5.11E-06
1441518_at	---	---	-10.82	1064.07	5.27E-06
1429197_s_at	RAB GTPase activating protein 1-like	Rabgap1l	-10.68	1052.27	5.38E-06
1450994_at	Rho-associated coiled-coil containing protein kinase 1	Rock1	-1.58	1017.9	5.75E-06
1438324_at	RIKEN cDNA 9330182L06 gene	9330182L06Rik	-4.03	989.176	6.09E-06
1456789_at	zinc finger protein 462	Zfp462	-30.27	966.047	6.39E-06
1420509_at	serum response factor binding protein 1	Srfbp1	-1.49	961.961	6.44E-06
1442075_at	expressed sequence AI314604	AI314604	-2.35	907.217	7.24E-06
1460256_at	carbonic anhydrase 3	Car3	-2.73	902.66	7.31E-06
1427263_at	inactive X specific transcripts	Xist	-65.79	900.544	7.34E-06
1449434_at	carbonic anhydrase 3	Car3	-4.94	860.593	8.04E-06
1453101_at	kelch-like 25 (Drosophila)	Klhl25	-6.26	799.136	9.32E-06
1443153_at	---	---	-2.15	792.443	9.47E-06
1454714_x_at	predicted gene, EG665516 /// predicted gene, EG666036 /// predicted gene, EG6687	EG665516 /// Phgdh	-120.48	768.03	1.01E-05
1440279_at	thioredoxin domain containing 10	Txndc10	-1.723	767.929	1.01E-05
1427144_at	heterogeneous nuclear ribonucleoprotein L-like	Hnrpll	-104.21	732.343	1.11E-05
1422952_at	Ng23 protein	Ng23	-4.56	722.632	1.14E-05
1431297_a_at	RIKEN cDNA 4933436C20 gene	4933436C20Rik	-9.35	722.363	1.14E-05
1417135_at	serine/arginine-rich protein specific kinase 2	Srpk2	-1.52	705.92	1.19E-05
1435397_at	zinc finger and BTB domain containing 44	Zbtb44	-3.55	690.991	1.24E-05
1424607_a_at	predicted gene, 100039204 /// predicted gene, 100040620 /// predicted gene, 1000	Cwc22 /// LOC100047648	-8.86	676.682	1.30E-05
1436364_x_at	nuclear factor I/X	Nfix	-5.87	670.024	1.32E-05
1455281_at	WD repeat domain 33	Wdr33	-2.05	654.554	1.39E-05
1451356_at	acidic (leucine-rich) nuclear phosphoprotein 32 family, member E	Anp32e	-1.38	641.68	1.44E-05
1425471_x_at	---	---	-3.45	624.285	1.52E-05
1419381_at	telomeric repeat binding factor 2, interacting protein	Terf2ip	-1.64	605.428	1.62E-05
1443932_at	kelch domain containing 1	Klhdc1	-24.23	603.745	1.63E-05
1436627_at	DNA segment, Chr 17, ERATO Doi 663, expressed	D17Ertd663e	-2.13	601.299	1.64E-05
1418843_at	solute carrier family 30 (zinc transporter), member 4	Slc30a4	-2.71	599.024	1.65E-05
1429621_at	cullin-associated and neddylation-dissociated 2 (putative)	Cand2	-12.14	586.08	1.73E-05

*F ratio and corresponding p value as determined by one-way ANOVA. F is the ratio of the mean of the squares between cohorts to the mean of the squares within each cohort.
Only the top 105 genes are shown. Primary data are available in the Gene Expression Omnibus database under accession number GSE16751.

Table S3: *Supplemental information on experimental methods and techniques*

Oligonucleotides used and conditions for PCR and sequencing

AID	Forward	5’-AAATGTCCGCTGGGCCAA-3’
	Reverse	5’-CATCGACTTCGTACAAGGG-3’
Hprt	Forward	5’-GGGGGCTATAAGTTCTTTGC-3’
	Reverse	5’- TCCAACACTTCGAGAGGTCC-3’
Arghgap26	Forward	5’-TCCATGACAACTGCTGCTTC-3’
	Reverse	5’-AAAATCCAATGGCCTCCTCT-3’
Blnk	Forward	5’-TCCATCAAAAGCCTGTACCC-3’
	Reverse	5’-AAACGATCCATCCTTGTTGG-3’
Cdkn1a	Forward	5’-TGAATACCGTGGGTGTCAAA-3’
	Reverse	5’-GTGTGAGGACTCGGGACAAT-3’
Rhob	Forward	5’-CTATGTGGCGGACATCGAG-3’
	Reverse	5’- TTGGGGCAGAAGTGCTTTAC-3’
Rhoh	Forward	5’-TGAACAAGCTTTCTGCATGG-3’
	Reverse	5’-ATGGCATAGTTGGGAAATGC-3’
Ubqln2	Forward	5’-TCCCAGGAGTAGCTCCACAC-3’
	Reverse	5’-CGAAAGCATGCTCTGAACAA-3’
Flnb	Forward	5’-TCAGCAAACAGGTTTTCCAG-3’
	Reverse	5’-GTGGGTGGCCCTAGTAAAAA-3’
Pax5	Forward	5’-GGAGGAGTGAATCAGCTTGG-3’
	Reverse	5’-TACTGAGGGTGGCTGTAGGG-3’
Pim1	Forward	5’-GGAGGAGTGAATCAGCTTGG-3’
	Reverse	5’-TACTGAGGGTGGCTGTAGGG-3’
Rhoh	Forward	5’-ACTCACTTCGGCACAGGAAC-3’
	Reverse	5’-CTAAGGGAATGTCCGTGGAA-3’.
BCR-ABL1	Forward 1st	5’-CAGAACTCGCAACAGTCCTT-3’
	Reverse 1st	5’-CTTGATGGAGAACTTGTTGTAGG-3’
	Forward 2nd	5’-CGAGTTGGTTCATCATCATTC-3’
	Reverse 2nd	5’- CTTGATGGAGAACTTGTTGTAGG-3’

Quantitative RT-PCR

Quantitative real time RT-PCR was carried out with SYBRGreenER mix (Invitrogen). Expression data was normalized against murine *Hprt* controls (Primer sequences listed above). For confirmatory quantitative real time RT-PCR, RNA was reverse transcribed to cDNA using Superscript III Reverse Transcriptase (Invitrogen). **Data are shown as a percentage of murine *Hprt* gene expression. For each gene, 5 AID$^{-/-}$ samples and 5 AID$^{+/+}$ samples from different mice were analyzed.**

PCR amplification and sequencing

PCR reactions were performed with Phusion polymerase (New England Biolabs, Cambridge, MA) using either 50ng genomic DNA template (*BCR-ABL1*, *Rhoh*, *Pim1*, and *Flnb*) or cDNA (*Pax5*). Amplification of *BCR-ABL1* was done with two rounds of PCR, in the first round the fusion oncogene was amplified followed by amplification of the *ABL1* kinase domain. Product DNA was purified using Minielute columns (Qiagen, Valencia, CA) and then cloned with the TOPO TA Cloning Kit as per manufacturer’s instructions (Invitrogen). Briefly, PCR product was cloned into the pCR4-TOPO vector at room temperature for 30 minutes. Following transformation of TOP10 chemically competent bacteria (Invitrogen), colonies were picked for subsequent colony PCR with the provided M13 primers using Phusion DNA polymerase. DNA sequencing on products was performed with T3 and T7 primers using an ABI 3730 DNA Analyzer.

Expression vectors and viral transduction

The MSCV-P190 BCR-ABL1-PGK-NEO vector was kindly provided by Dr. Richard Van Etten, Tufts University. Retroviral supernatant was produced by transient transfection of 293T cells as previously described (18).

Mouse bone marrow transplants

Bone marrow of male Balb/c AID$^{+/+}$ or AID$^{-/-}$ mice was harvested and cultured in the presence of 10 ng/ml murine interleukin-7 (mIL-7) and 50 ng/ml murine Flt3 ligand (mFlt3L) for 48 hours prior to transduction on RetroNectin (Takara Bio Inc.) coated plates. 24 hours following transduction cells were harvested and transplanted into lethally irradiated female Balb/c recipients (900 Gy in two fractions separated by 12 hours) at a dose of 10^6 cells per mouse via intravenous injection. Mice were treated for 21 days post transplant with tetracycline administered through the drinking water as a prophylactic measure while they are immunocompromised (200 μg/ml). Leukemia cells from sacrificed mice were recovered from the peripheral blood and spleen and purified by CD19 MACS microbead technology (Miltenyi Biotec). These cells were maintained in IMDM supplemented with 50 μmol/l 2-mercaptoethanol and 10% fetal bovine serum until they were transplanted into secondary recipients. For secondary transplants, recipients were conditioned with lethal irradiation as described above. 10^4 leukemia cells were injected intravenously along with 10^6 bone marrow cells from Balb/c mice harvested 24 hours prior and maintained in 10 ng/ml murine interleukin-3 (mIL-3), 2.5 ng/ml murine stem cell factor (mSCF), and 25 ng/ml murine interleukin-6 (mIL-6) overnight.