

Supplemental Information

Jmjd1c is Required for MLL-AF9 and HOXA9 Mediated AML Stem Cell Self-Renewal

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Figure S1

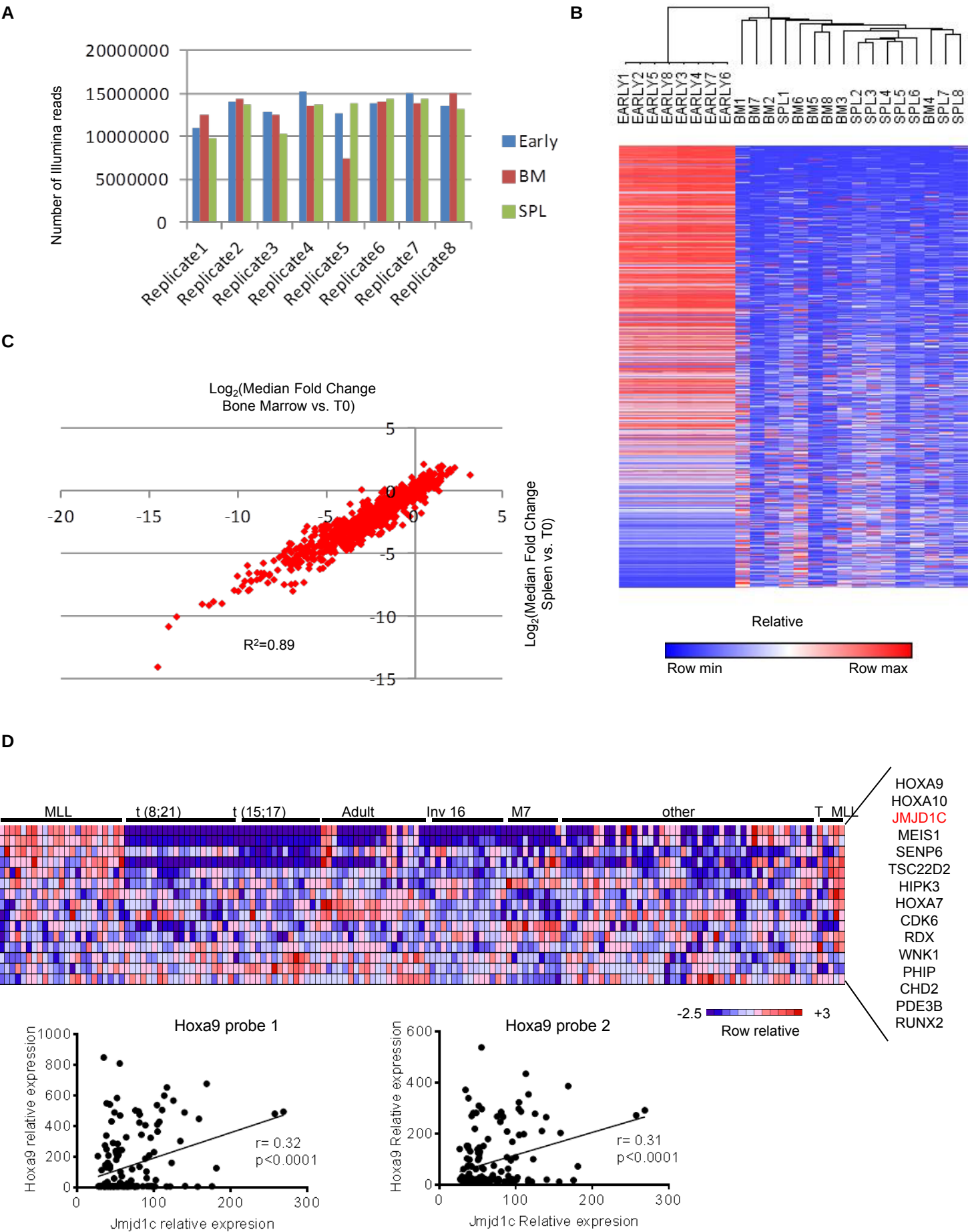


Figure S1. In vivo shRNA screen of MLL-AF9 targets. Related to Figure 1.

(A) Number of reads obtained from Illumina sequencing of eight experimental replicates. (B) Unsupervised hierarchical clustering of normalized reads of all hairpins in eight replicates. Hairpins are ranked by their depletion level in the bone marrow using log₂ median fold-change. (C) Scatter plot showing correlation of Log₂ Fold Change in the BM vs. SPL. (D) Heatmap of MLL-AF9 target genes (14) (upper panel) and scatter plot of Hoxa9 and Jmjd1c expression level (bottom panel) in human leukemias (39).

Figure S2

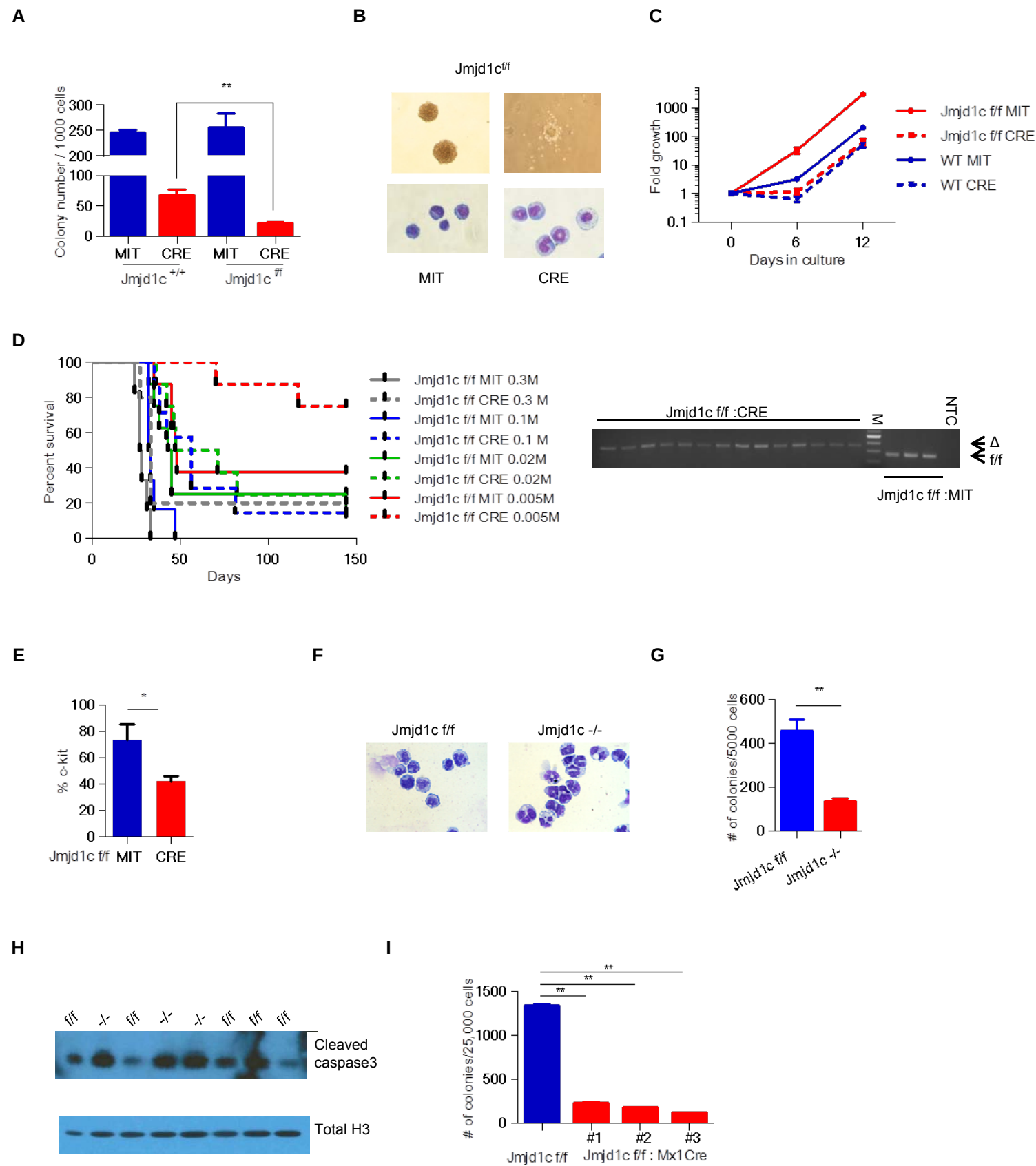
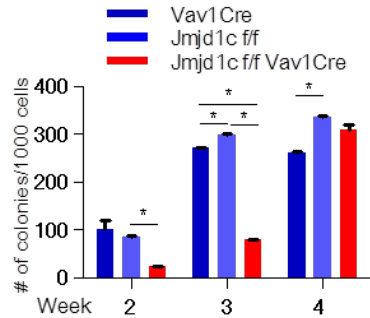
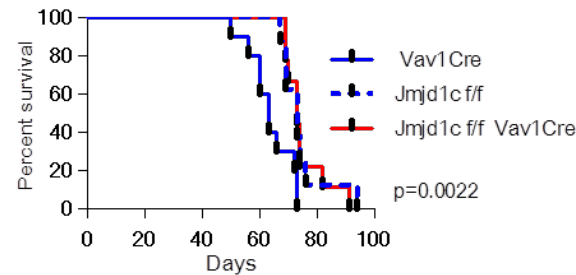


Figure S2 continued

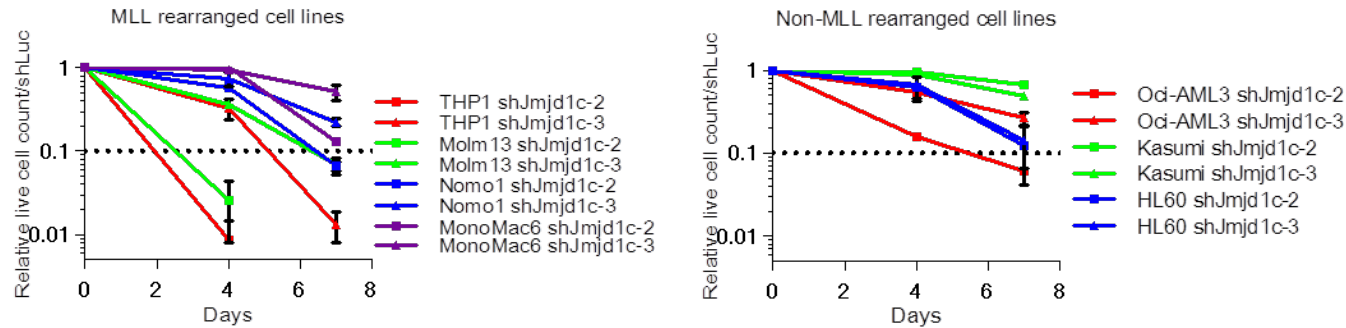
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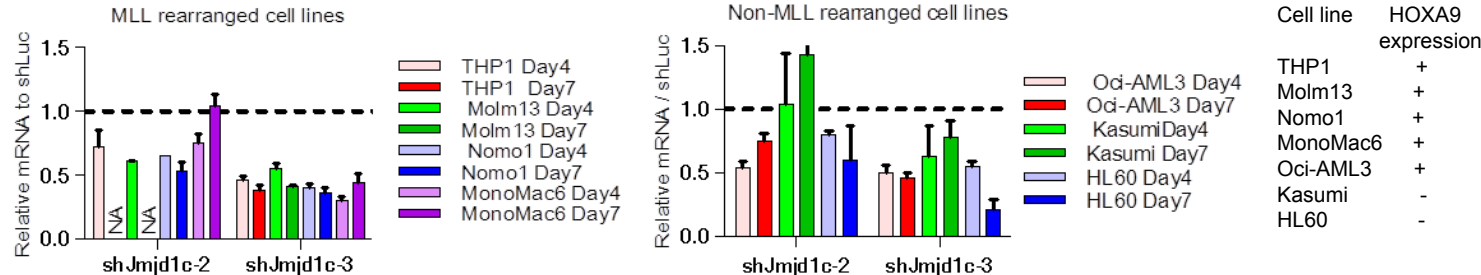
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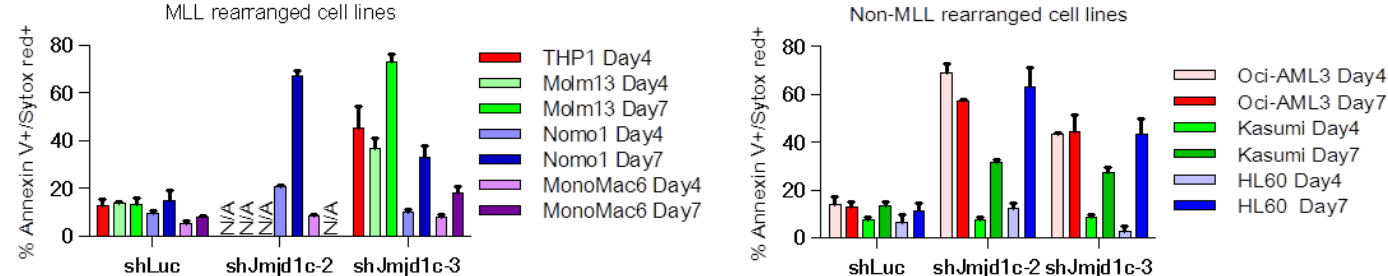
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M



N



O

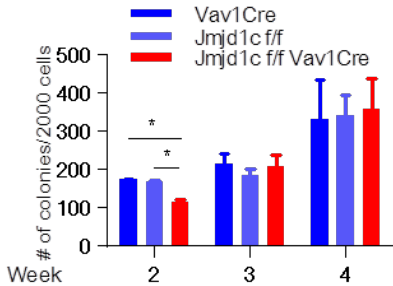
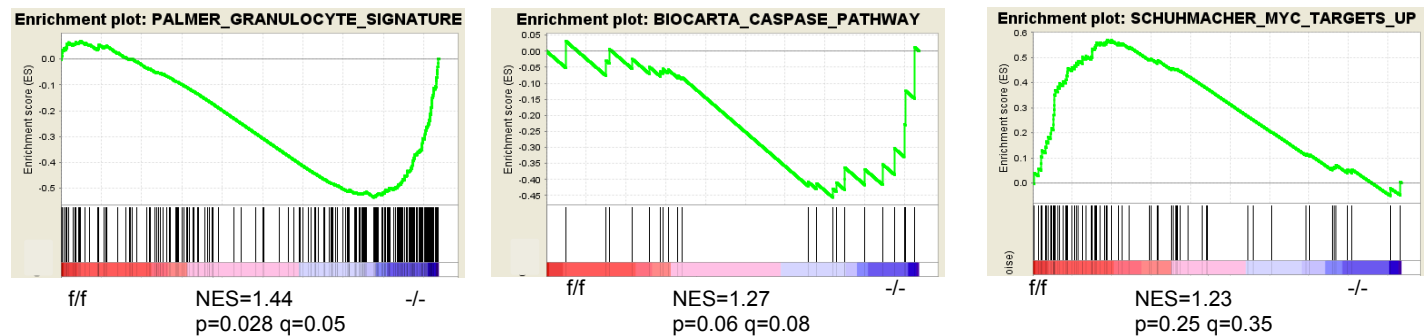


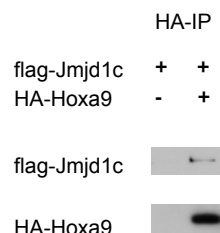
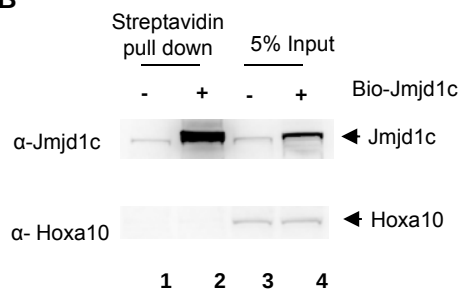
Figure S2. Effect of loss of Jmjd1c in MLL-AF9 leukemia. Related to Figure 2&3. (A) Colony counts of MLL-AF9 transformed pre-leukemic cells derived from *Jmjd1c^{ff}* and *wt* background 7 days after transduction of CRE or MIT control viruses in methylcellulose. Results from two to three independent experiments. (B) Morphology 9 days after CRE transduction: colony image (top [x40 original magnification]) and Wright- Giemsa staining (bottom [x400 original magnification]). (C) Proliferation assay of sorted GFP+/Tomato+ MLL-AF9 leukemia cells from *Jmjd1c^{ff}* (triplicate samples from three leukemias) and *wt* (triplicate samples) background after transduction with MIT control or CRE virus. (D) Limiting dilution transplantation of cells in (C) see also Table S1. Right panel: Genotyping PCR of BM cells. (E)-(H) Analysis of BM cells from secondary recipient mice. (E) Flow cytometry analysis of c-Kit expression, n=4&7 for *Jmjd1c* MIT & CRE in BM cells from secondary recipients as in (D). (F) Wright-Giemsa staining of sorted GFP+/Tomato+ (*Jmjd1c^{-/-}*) or GFP+ (*Jmjd1c^{ff}*) MLL-AF9 leukemia cells from secondary recipients (x400 original magnification), Colony counts of sorted leukemic cells as in (F) in methylcellulose after 7 days. Duplicate samples from two leukemias are shown. (H) Western blot of cleaved caspase 3 in BM cells as in (F). (I) Colony counts of sorted peripheral blood GFP+ cells in methylcellulose after 7 days from mice transplanted in Figure 3B 29 days after plpC administration. Duplicate samples from three plpC treated *Jmjd1c^{ff} : Mx1Cre* leukemias and a non-treated leukemia are shown. (J) Colony counts of MLL-AF9 transformed pre-leukemic cells derived from *Jmjd1c^{ff}:Vav1Cre* and controls. Shown are duplicate samples. (K) Survival curve of primary recipient mice that received 3,000 MLL-AF9 transformed LSKs from *Jmjd1c^{ff}: Vav1Cre* and controls. (L) Proliferation of human leukemia cells transduced with shRNA (two independent shRNAs were used) against *Jmjd1c* compared to shLuc control, as measured by live cell counts. Results from four independent experiments. (M) RT-QPCR performed using cells from (L). Results from three independent experiments. (N) Apoptosis assay of transduced cells as in (L). Shown are duplicate samples. Color key same as in (L) and different shades of the same color represents different time point: lighter day4 and darker day7. NA: no day7 data available because of insufficient number of cells. (O) Colony counts of *Hoxa9/Meis1* transformed pre-leukemic cells derived from *Jmjd1c^{ff}:Vav1Cre* and controls. Results from two independent experiments in duplicates. Data are represented as mean $\pm$ SEM in (A), (E), (G), (I), (J) & (L)-(O). *p<0.05; **p<0.01 student's t-test.

Figure S3

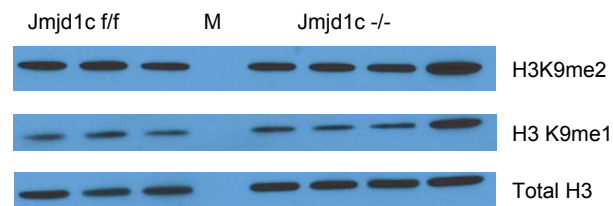
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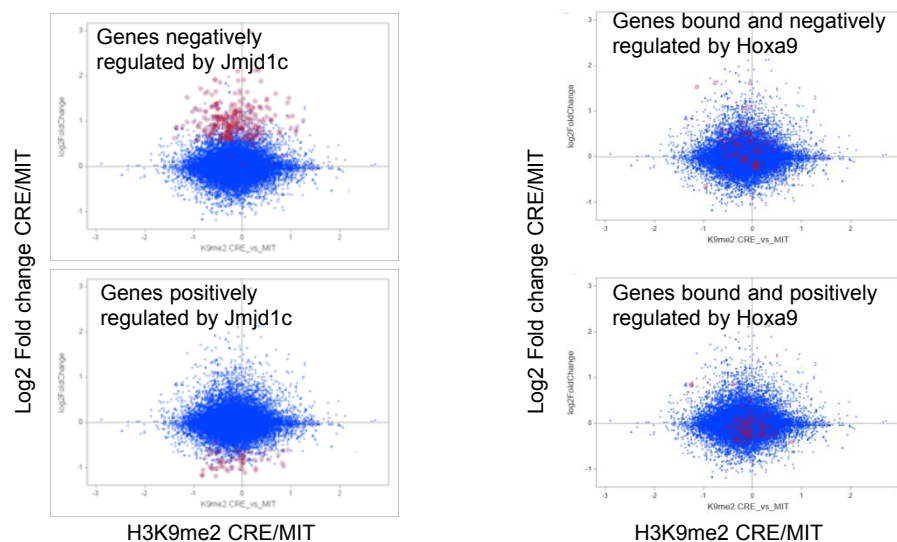
B



C



D



E

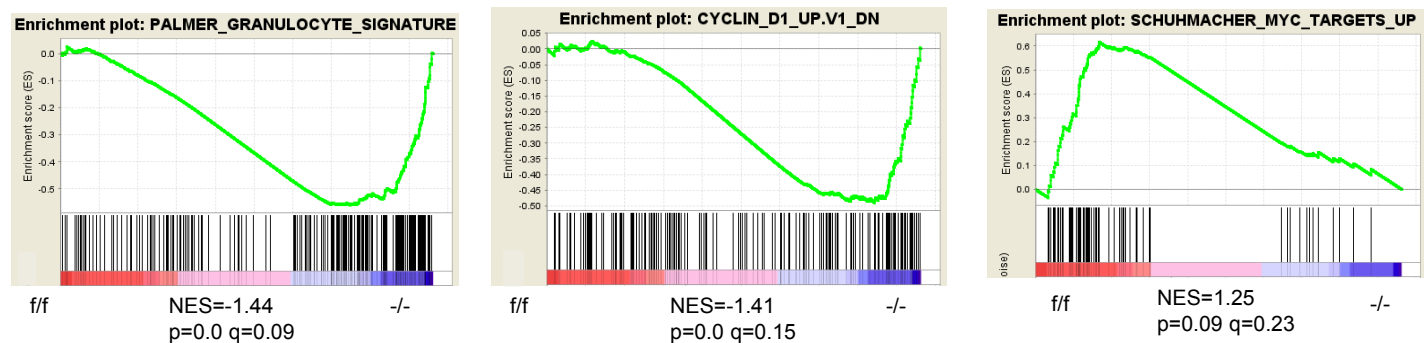
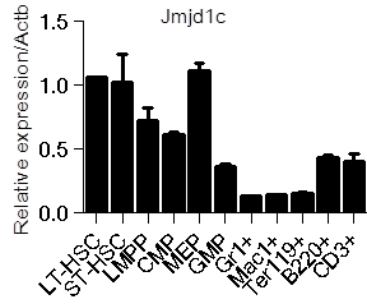


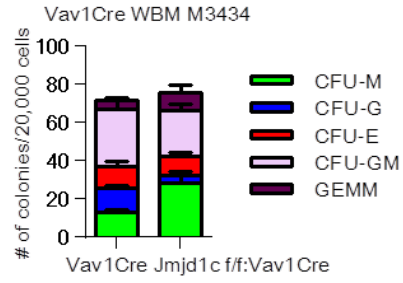
Figure S3. Loss of Jmjd1c on gene expression and histone methylation. Related to Figure 4. (A) GSEA analysis result showing enrichment of differentiation and apoptosis pathway in MLL-AF9 leukemia cells 6 days after loss of Jmjd1c. (B) Left panel : Co-immunoprecipitation of HOXA10 and JMJD1C in 293T cells transfected with indicated plasmids. Right panel: In vitro protein-protein interaction assay between purified HA-Hoxa9 from 293T cells and baculovirus system expressed and purified flag-Jmjd1c. (C) Western on H3K9me2/me1 in BM cells from secondary MLL-AF9 recipient mice. (D) Scatter plots of Log2 gene expression changes (CRE/MIT Y axis) vs. H3K9me2 level. Highlighted in red populations: upper left: genes that are up-regulated upon loss of Jmjd1c; lower left: genes that are down-regulated upon loss of Jmjd1c; upper right: genes that are bound and repressed by Hoxa9; lower right: genes that are bound and activated by Hoxa9 (44). (E) GSEA analysis result showing enrichment of differentiation and negative regulation of cell cycle signatures in Hoxa9/Meis1 leukemia cells 6 days after loss of Jmjd1c.

Figure S4

A



C



B

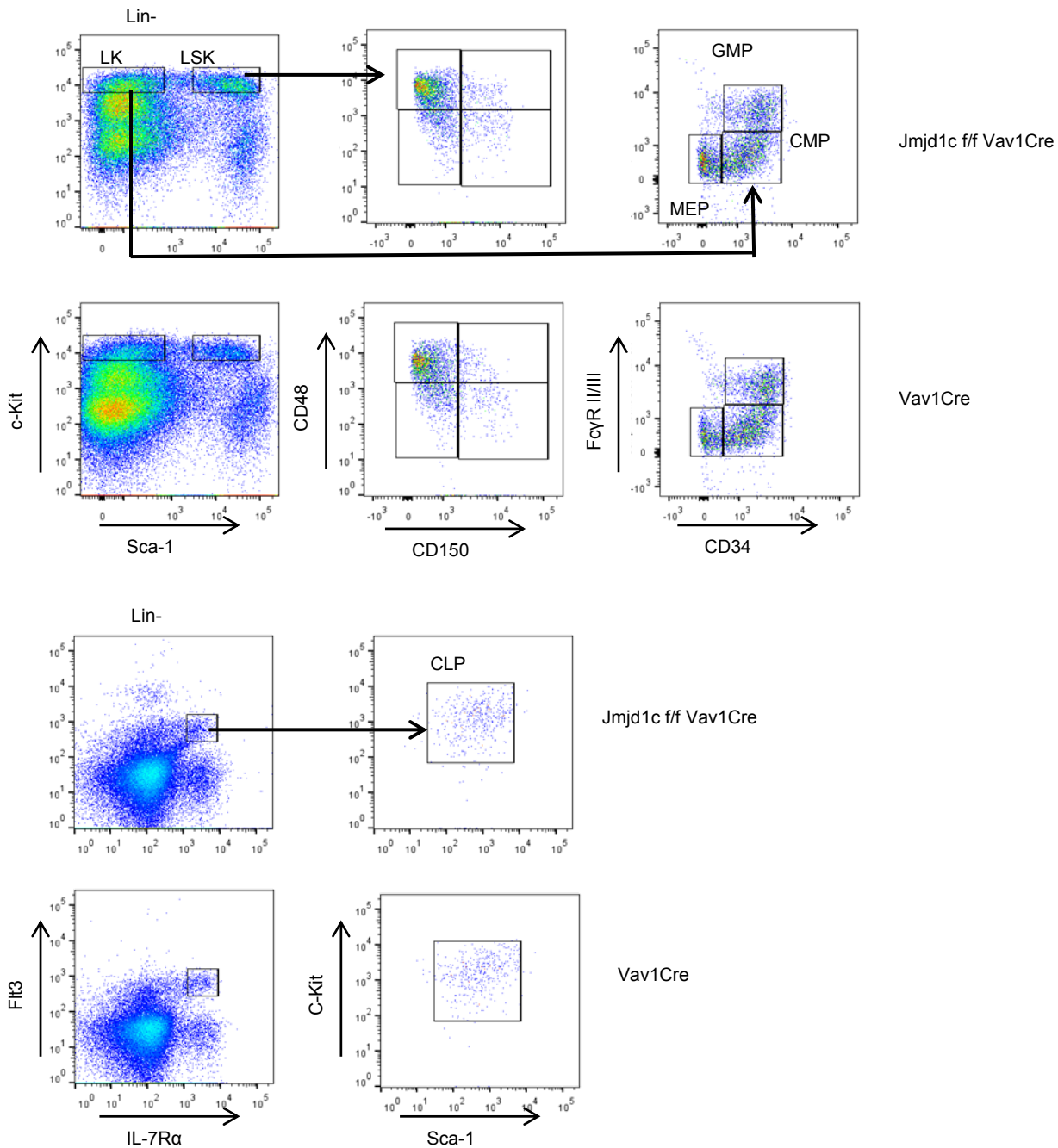


Figure S4. Effect of loss of Jmjd1c in normal hematopoiesis. Related to Figure 6.

(A) RT-QPCR analysis of Jmjd1c level in hematopoietic compartments (n=3 biological replicates). LT-HSC [LSK Flt3-CD34⁻], ST-HSC [LSK Flt3-CD34⁺], LMPP [LSK Flt3⁺CD34⁺], CMP [LK CD34⁺FcγR II/III^{lo}], GMP [LK CD34⁺FcγR II/III^{hi}], MEP [LK CD34-FcγR II/III^{lo}]. (B) Colony formation of normal hematopoietic progenitors using whole bone marrow from *Jmjd1c^{fl/fl};Vav1Cre* mice. Summary of three independent experiments. (C) Representative stem progenitors flow cytometry plots from *Jmjd1c^{fl/fl};Vav1Cre* (top panel) and *Vav1Cre* (bottom) mice (LK [Lin⁻c-Kit⁺], CLP [Lin⁻IL7R⁺Flt3⁺Sca-1^{lo}c-Kit⁺], HSC [LSK CD150⁺CD48⁻]). Data are represented as mean± SEM in (A)&(C).

Figure S5

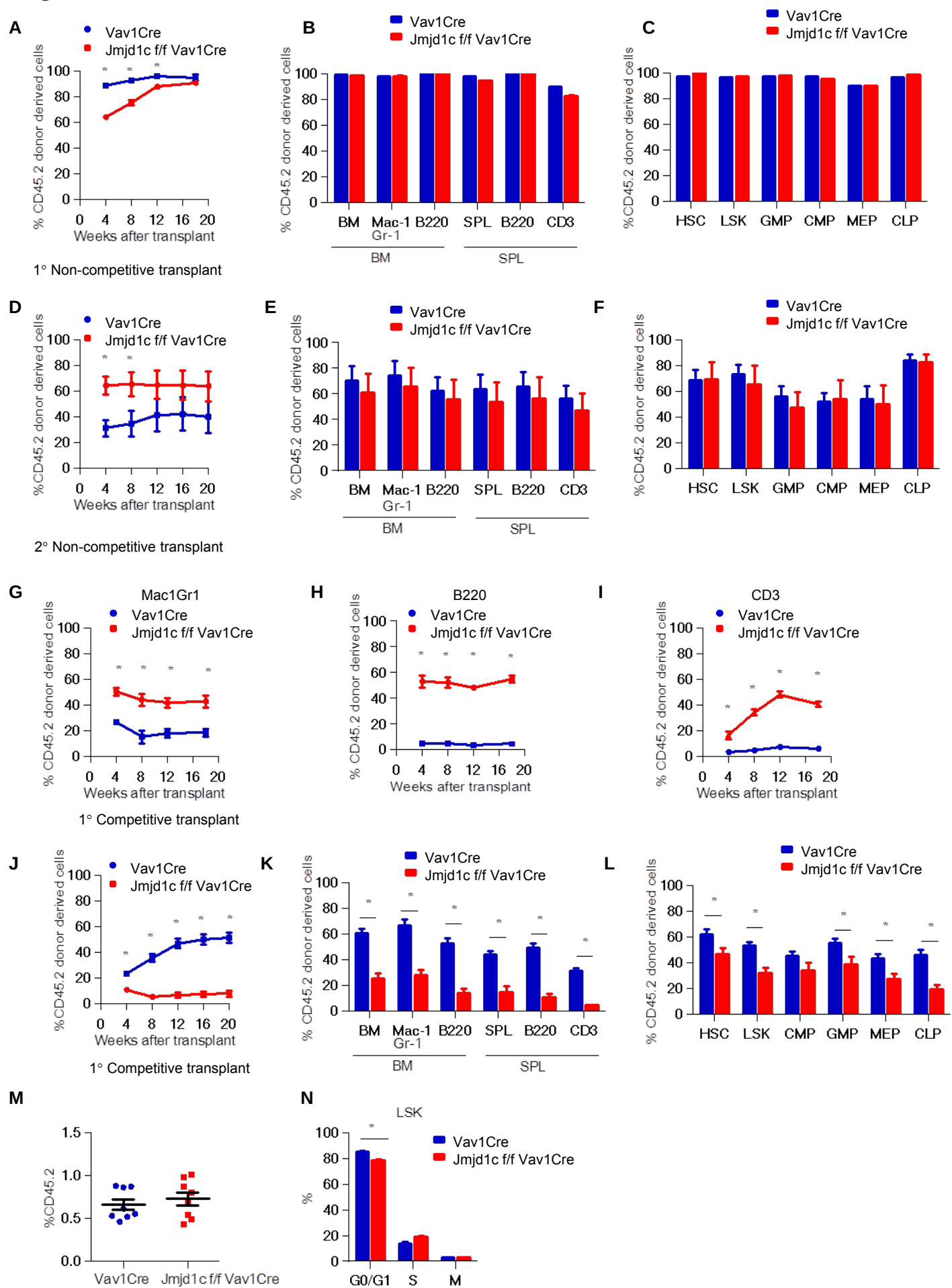


Figure S5 continued

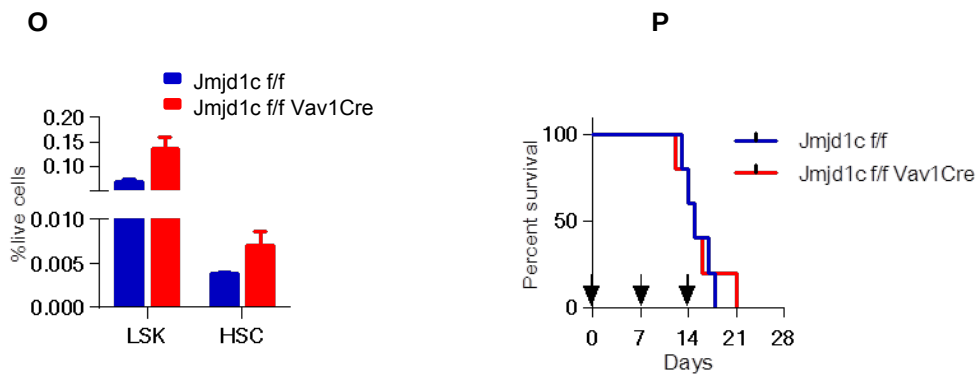


Figure S5. Effect of loss of *Jmjd1c* in regenerative hematopoiesis. Related to Figure 7. (A)-(L) Flow cytometry analysis results of chimerism of recipient mice from transplantation experiments. (A)-(C) Two million BM cells from *Vav1Cre* or *Jmjd1c^{ff} : Vav1Cre* were transplanted into lethally irradiated CD45.1 recipients. (n=10) (D)-(F) Two million BM cells from primary non-competitive transplantation were serially transplanted into secondary CD45.1 recipients (n=10). (G)-(I) Chimerism of PB Mac-1 Gr-1(G), B220 (H) and CD3 (I) in primary competitive transplant as in Figure 7(A)-(C). (J)-(K) Two hundred HSC (CD150⁺CD48⁻Lin⁻Sca-1⁺c-Kit⁺) cells from *Vav1Cre* or *Jmjd1c^{ff} : Vav1Cre* were mixed 1:1 with 200 CD45.1 HSC cells plus 0.2 million CD45.1 helper cells and transplanted into lethally irradiated CD45.1 recipients. (n=15). Chimerism in peripheral blood (A),(D),(G)-(I)&(J); bone marrow and spleen (B),(E)&(K); stem and progenitor populations in BM (C),(F)&(L). (M) Homing of whole bone marrow from *Jmjd1c^{ff} : Vav1Cre* mice analyzed 18 hours after transplantation (n=8). Two donor mice and eight recipients were used. (N) Cell cycle analysis by BrdU and Sytox blue (n=3 per genotype). (O) HSPC frequency two weeks after 5-Fu treatment (n=3-4 per genotype). (P) Survival curve of *Jmjd1c^{ff} : Vav1Cre* mice after weekly 5-Fu treatment (indicated by arrows) (n=5 per genotype). Data are represented as mean $\pm$ SEM. *p<0.05 student's t-test.

Figure S6

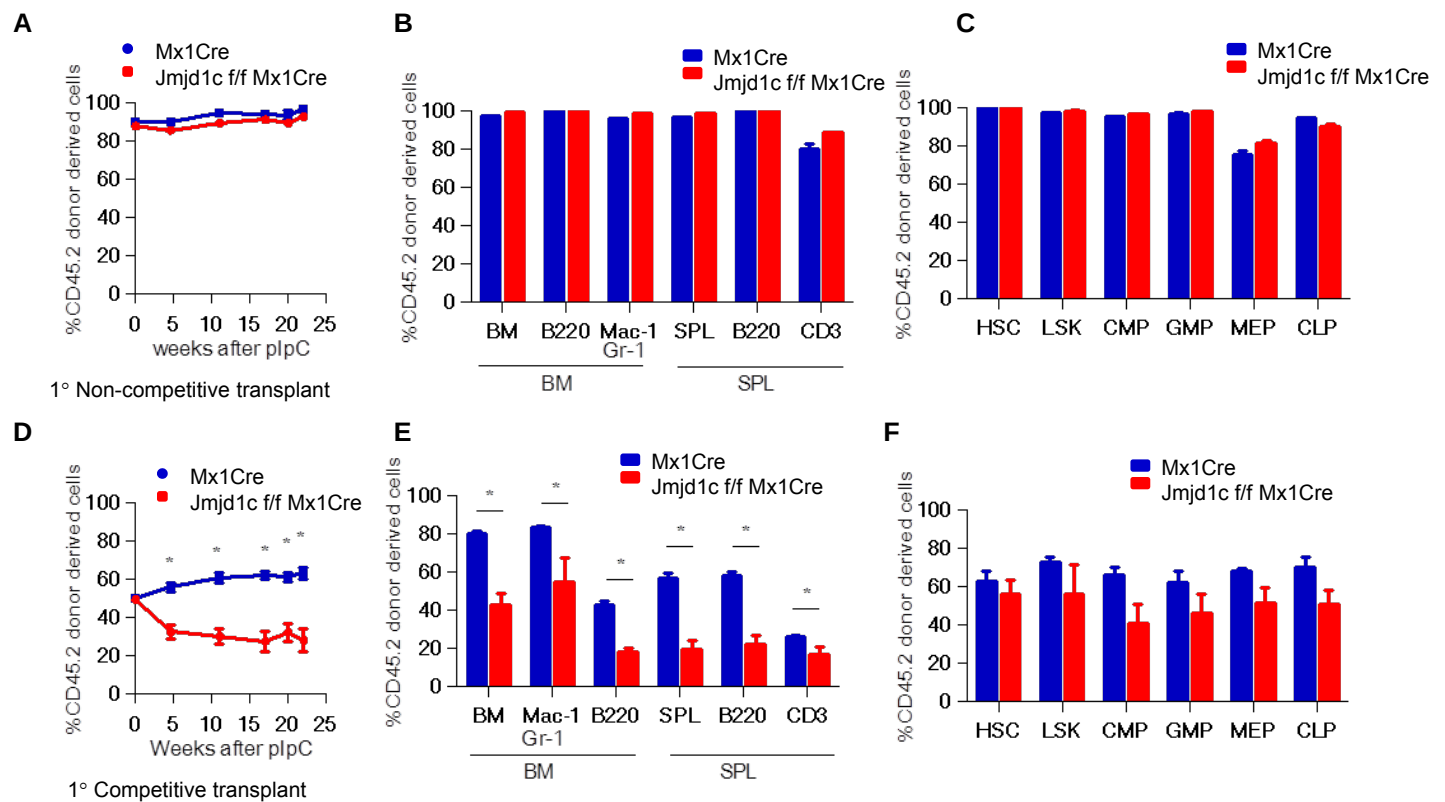


Figure S6 Characterization of loss of Jmjd1c in regenerative hematopoiesis using Mx1Cre system. Related to Figure 7.

(A)-(C) Two million BM cells from *Mx1Cre* or *Jmjd1c*^{f/f} : *Mx1Cre* were transplanted into lethally irradiated CD45.1 recipients (n=5). (D)-(F) One million BM cells from *Mx1Cre* or *Jmjd1c*^{f/f} : *Mx1Cre* were mixed 1:1 with CD45.1 BM and transplanted into lethally irradiated CD45.1 recipients (n=5). Chimerism in peripheral blood (A)&(D) ; bone marrow and spleen (B)&(E); stem and progenitor populations in BM (C)& (F). Data are represented as mean± SEM. *p<0.05 student's t-test.

Supplemental Tables

Table S1. Related to Figure 1. Genes Targeted in the shRNA Screen.

1110003E01Rik	Cdkn1b	Fut8	Lass2	Pgd	Six1
1110034A24Rik	Cenpv	Gda	Lass6	Phtf1	Six4
1110059E24Rik	Chd2	Gfi1	Lmo2	Pigl	Slc38a1
2410002O22Rik	Chd7	GFP	Lnpep	Pitpnc1	Sltn
2810407C02Rik	Chd9	Gm7120	Lrrc33	Poli	Smc4
4931408C20Rik	Copb1	Gxylt1	Lta4h	Prkar2b	Snx13
Aff1	Crif3	Hectd1	LUCIFERASE	Psma1	Snx9
AI314180	Ctnnb1	Hhex	March7	Pus10	Sos2
Ankib1	D930015E06Rik	Hjurp	Mbnl1	Rap1gds1	Stxbp5
Ano6	Dach1	Hnrpl	Meis1	Rdx	Supt3h
Arhgap19	Dcun1d1	Hoxa10	Mgat2	Reep3	Susd1
Arid1b	Dirc2	Hoxa11	Mgat5	Rev1	Tmem181a
Arid2	Dock8	Hoxa3	Mppe1	RFP	Tnpo1
Arih2	Dsp	Hoxa7	Mrp63	Rhob	Trim23
Atp11b	Eif2a	Hoxa9	Mtus1	Rnf13	Trim59
B3gnt2	Eif5b	Hpgd	Myb	Rnf220	Trip4
B4galt6	Elf1	Hsd17b11	N4bp2	Rod1	Trpm8
Baz1a	Emb	Ift80	Naa16	Rpl36a	Tsc22d2
Baz2b	Erbp2ip	Ikzf1	Ncor1	Rreb1	Ube2k
Bcor	Etv6	Il12a	Nipbl	Rsb1l	Ugt1a1
Bfsp1	F630043A04Rik	Jmjd1c	Npr1	Runx2	Vcpip1
Cacnb2	Fam108b	Kctd1	Nrg2	Satb2	Vps54
Cbx3	Fam63a	Kif11	Parp8	Serp1	Wbp4
Cd47	Fcho2	Klhdc2	Pde3b	Sfi1	Zcchc2
Cdk17	Fhdc1	Krit1	Pds5a	Sgk3	
Cdk6	Frat2	lacZ	Pex13	Siah2	

Table S2. Related to Figure 1. Positive hits in the shRNA screen

Gene Symbol	#shRNAs Depleted >10-fold in BM
March7	3
1110003E01Rik	3
1110034A24Rik	3
2810407C02Rik	2
Ano6	3
Arid1b	4
Arid2	2
Atp11b	3
B4galt6	3
Bcor	3
Cbx3	4
Cdk17	4
Cenpv	3
Chd2	2
Chd7	2
Copb1	4
D930015E06Rik	3
Dcun1d1	2
Dirc2	2
Eif2a	4
Eif5b	5
ErbB2ip	2
Etv6	2
Fam63a	2
Fhdc1	2
Gda	2
Gfi1	3
Gm7120	3
Gxylt1	3
Hectd1	5
Hhex	2
HnrpII	4

Gene Symbol	#shRNAs Depleted >10-fold in BM
Hoxa10	2
Hoxa11	2
Hoxa9	4
Hsd17b11	2
Ift80	3
Il12a	2
Jmjd1c	3
Kif11	4
Klhdc2	3
Lass2	4
Lmo2	2
Lrrc33	3
Meis1	3
Mgat2	2
Mppe1	3
Mrp63	2
Mtus1	3
Ncor1	2
Nipbl	2
Npr1	2
Nrg2	3
Parp8	4
Pds5a	4
Pex13	3
Phtf1	3
Pitpnc1	3
Poli	2
Prkar2b	3
Psma1	3
Pus10	3
Rap1gds1	2
Rdx	4

Gene Symbol	#shRNAs Depleted >10-fold in BM
Reep3	2
Rev1	5
Rnf13	2
Rod1	2
Rreb1	3
Rsb1l	3
Satb2	2
Serp1	2
Sfi1	3
Siah2	3
Six1	3
Six4	3

Gene Symbol	#shRNAs Depleted >10-fold in BM
Smc4	3
Sos2	2
Supt3h	3
Tnpo1	2
Trim59	2
Tsc22d2	2
Ube2k	2
Ugt1a1	3
Vcpi1	3
Vps54	3
Wbp4	2
Zcchc2	2

Table S3. Limiting dilution assay result of MLL-AF9 leukemia

Dose	Response/Tested		P value
	MIT	CRE	MIT vs Cre
300,000	6/6	4/5	0.0476
100,000	6/6	6/7	0.0007
20,000	7/8	6/8	0.3266
5,000	5/8	2/8	0.044
LIC frequency	1 in 7,000	1 in 53,000	

Table S4. Related to Figure 3. Differentially regulated genes (fold> 1.5, p<0.05), between Jmjd1c^{ff} and Jmjd1c^{-/-} MII-AF9 leukemic cells

Gene Symbol	Log2 fold change	Adjusted p value
Jmjd1c	-1.04466	1.11E-15
Slc28a2	-0.78389	1.72E-06
Cbx6	-0.81636	3.76E-06
Celsr1	-1.06829	4.78E-06
Pak1	-0.81927	6.94E-06
Gm14085	-0.79653	1.98E-05
Ascl2	-1.11069	2.92E-05
Cbs	-1.16428	5.35E-05
Ogdhl	-0.98726	0.000307
Fam212a	-0.99038	0.000422
Snhg4	-0.66807	0.000825
Ms4a3	-0.81898	0.000942
Wdr34	-0.83871	0.000963
Adrbk2	-1.22063	0.001219
B4galnt4	-0.9639	0.001394
Megf8	-0.6973	0.001532
Sarm1	-1.05753	0.001625
Dancr	-0.63142	0.001625
Doc2g	-0.67437	0.001681
Rab34	-0.98188	0.004112
Tbc1d16	-0.70577	0.004582
Smpd3	-0.89456	0.005552
Nefh	-0.89013	0.006075
Spag4	-0.88346	0.006538
Fam69b	-0.67687	0.006584
Bcl7a	-0.77939	0.008908
Gga2	-0.61331	0.010834
Lmo1	-0.97932	0.011071
Elfn2	-1.01907	0.013178
Sh2d5	-0.68103	0.014798
Lzts2	-0.64126	0.016256
Gtdc2	-0.8075	0.01841

Gene Symbol	Log2 fold change	Adjusted p value
Arhgef10	-0.9222	0.02177
Slc29a2	-0.63404	0.022054
Arhgef25	-0.85623	0.024187
Samd4	-1.04005	0.026193
Snord47	-0.78796	0.026193
Gspt2	-1.06042	0.027138
Prickle1	-0.71359	0.028597
Art5	-0.7898	0.029591
5033406O09Rik	-0.59476	0.031161
Cdh17	-0.97635	0.032531
Acer2	-0.72275	0.033876
Arxes2	-1.0474	0.034475
Pcdhgb4	-0.61768	0.036737
Pcdhga1	-0.64403	0.037102
Cftr	-1.04029	0.038276
Ltbp4	-0.88001	0.043665
Bhlhb9	-0.79316	0.043665
Rtn4r	-0.74631	0.043718
Pcdhgb5	-0.6041	0.043865
Unc79	-0.82573	0.04415
Pcdhgb6	-0.59251	0.04469
Alms1-ps2	-0.70529	0.047744
Cabp1	-0.97949	0.048913
Pcdhga2	-0.61616	0.048913
Gria3	-0.66066	0.049001
Itgb3	2.123955	9.85E-37
Abca1	2.998431	7.33E-25
Rcbtb2	0.91221	3.1E-22
Ablim1	1.932867	8.2E-20
Gas7	1.633059	2.56E-18
Abcg1	1.919096	1.28E-16
Thbd	1.469246	6.94E-13

Gene Symbol	Log2 fold change	Adjusted p value
Ptplad2	1.627055	5.91E-12
Galnt9	1.888043	5.07E-11
Clec4a3	2.155225	5.07E-11
Chn2	1.236862	1.14E-10
Tgfbr2	1.303205	1.59E-09
Emb	0.75423	3.03E-09
Hpse	1.421579	2.17E-08
Eps8	1.326527	2.23E-08
Bank1	1.374639	2.48E-08
Gapt	0.685839	2.82E-08
Arhgap24	1.39838	5.54E-08
Dab2	1.406241	1.01E-07
Sema4d	1.096698	1.06E-07
Milr1	1.051428	1.38E-07
Rab32	0.755518	1.83E-07
Tuba8	0.677924	2.51E-07
Tmcc3	1.674284	3.65E-07
Ptgs1	0.864621	6.66E-07
9130019P16Rik	1.11841	3.1E-06
Tpm4	0.940281	5.58E-06
Pik3c2g	1.714589	6.61E-06
Cd180	1.466262	7.33E-06
Dse	1.336947	7.41E-06
Irf8	1.212485	9.95E-06
Rgl1	1.652077	1.3E-05
Dpep3	1.458813	1.67E-05
Cd28	1.551472	1.88E-05
Psap	0.923304	2.74E-05
Siglec1	1.617327	3.09E-05
Ahr	1.225626	3.31E-05
Trps1	1.099351	4.32E-05
Cytip	0.783734	7.57E-05

Gene Symbol	Log2 fold change	Adjusted p value
P2rx7	1.340745	8.14E-05
Clec4a1	1.342085	0.000106
P2ry6	1.365247	0.000106
Rassf4	0.885495	0.000115
Gm6116	1.539708	0.000141
Itgb7	0.99194	0.000173
Casp6	0.641038	0.00018
Il15	1.220225	0.000191
St3gal1	0.764674	0.000222
Tlr9	1.346061	0.000232
Gm6904	1.525104	0.000267
Cdkn1a	0.812278	0.000301
Csf2rb	0.711743	0.000307
Cd93	0.87226	0.000307
Cd274	1.083347	0.000307
Mgst1	0.794224	0.000328
Rap2b	0.598355	0.000332
1810011H11Rik	0.697994	0.000422
Gpr35	1.349269	0.000425
Ninj1	0.862573	0.000429
Tlr7	1.268991	0.000429
Tlr2	1.117165	0.000469
Myo1e	0.731512	0.000524
Tpd52	0.795116	0.000658
Neur13	0.797467	0.000751
Mafb	1.39057	0.00076
Vwa5a	0.869746	0.000832
Ssxb9	1.393362	0.000832
Gngt2	1.074443	0.000834
Cd164	0.676565	0.000963
Csf2rb2	0.772507	0.001022
Hmox1	0.855608	0.001022

Gene Symbol	Log2 fold change	Adjusted p value
Ston2	0.85642	0.001072
5430435G22Rik	1.068103	0.001097
Plk2	1.083151	0.001219
Tnfsf9	1.294997	0.001398
9030617O03Rik	0.710034	0.001428
Rgs2	0.731983	0.001446
Lrp1	1.142112	0.001532
Pde7b	1.254865	0.001532
Abcc3	0.941484	0.001666
5830416P10Rik	0.720318	0.001811
Trp53inp1	0.72678	0.002049
Camkk1	0.88428	0.002049
Nov	1.083977	0.002049
Prr5l	1.145204	0.002049
Htr2a	1.304739	0.002049
Sc5d	0.614511	0.002089
Mndal	1.017784	0.002089
Lair1	0.888594	0.002234
Slc9a9	0.879592	0.002291
Cpeb2	0.806953	0.002295
Kcnn4	0.90791	0.002295
Hao	0.724052	0.002468
Gm19689	1.33056	0.002559
Bmf	0.743496	0.002654
Ms4a7	1.305401	0.002813
Slc25a15	0.724929	0.002833
Tle3	0.70288	0.003359
Zfp608	0.848658	0.003426
Mr1	1.110452	0.003426
Ptafr	1.085053	0.003461
Cxcl12	1.293795	0.003794
Rara	0.914714	0.003802

Gene Symbol	Log2 fold change	Adjusted p value
Fblim1	1.117164	0.004057
Cd97	0.845226	0.004077
Smim3	0.665106	0.004112
Nos2	1.282475	0.004119
Hlx	0.879396	0.004226
Pde8b	0.871051	0.004439
Vwf	1.107922	0.004523
F13a1	1.142199	0.004582
Trem2	1.2626	0.004605
Ugt1a7c	0.627866	0.004815
A630033H20Rik	1.164218	0.004815
Gfra1	1.229251	0.004815
Gm5122	1.256649	0.004815
Tsc22d1	1.001162	0.004977
Angptl2	1.226805	0.005024
Gfi1b	1.23925	0.005038
Zmat3	0.730585	0.005082
Filip1l	0.65971	0.005143
Cd300lb	0.90606	0.005336
Sirpa	0.668059	0.00534
Mgam	0.862863	0.005526
Arhgef3	0.651612	0.006051
Gal	0.754296	0.006051
Mx2	1.190473	0.006051
Parp12	0.665018	0.006148
Ugt1a10	0.644697	0.006548
Ugt1a5	0.644595	0.006553
Ugt1a1	0.644979	0.006553
Ugt1a9	0.642828	0.006584
Ugt1a2	0.643657	0.006584
Fbp1	1.12143	0.006584
Ppt1	0.619918	0.00663

Gene Symbol	Log2 fold change	Adjusted p value
Ugt1a6b	0.643107	0.006657
Ugt1a6a	0.641147	0.007059
Clvs1	0.869823	0.008001
Ndst1	0.646302	0.00902
Ptk2b	0.59043	0.009555
Nxpe5	1.049813	0.009685
Arhgap31	0.682377	0.010654
AU022793	1.072586	0.010654
Il12rb2	0.603537	0.011552
A1cf	1.123558	0.011689
Trim9	0.605036	0.011826
Lct	0.753159	0.011826
Cgn	0.972843	0.011826
Emp1	1.151407	0.011826
Abhd5	0.585817	0.012392
Serpina3f	1.129434	0.013101
Smad3	0.623081	0.014868
Ube2l6	1.011999	0.016879
0610040F04Rik	0.964345	0.017685
C1qc	1.066999	0.018461
Krt80	0.880684	0.018551
Klk1b9	1.138404	0.018566
Adamts2	0.991314	0.022205
Irs2	0.593489	0.023754
A730020M07Rik	1.009852	0.024187
Rhov	0.878516	0.024343
Mefv	0.732721	0.025414
Oas3	0.822992	0.025414
Socs1	0.634574	0.025434
Igf1	1.072821	0.026193
Gm14005	0.848907	0.026588
Gbp7	0.667154	0.027126

Gene Symbol	Log2 fold change	Adjusted p value
Lrp12	0.724524	0.027126
Tcf7l2	0.915086	0.027138
AF251705	0.589143	0.027422
S100a4	1.040842	0.028074
Stat4	0.698032	0.02846
Gdpd5	0.629614	0.028699
BC021767	1.04356	0.028987
Ndrp1	0.655756	0.03125
Tubb1	1.048013	0.03125
Zc3h12d	1.077031	0.03125
Slc52a3	0.761571	0.031959
Lpar6	0.585153	0.032205
Asb2	1.062198	0.032225
Ap5s1	0.852437	0.033026
Siglec5	0.840631	0.033565
Rasgrp3	1.053262	0.033565
Klk1b4	1.066315	0.033565
Lif	0.978898	0.033876
Dennd2c	0.690892	0.033929
Krt86	0.889423	0.033929
Gng2	0.601272	0.03406
Ptpro	1.061994	0.03406
Klk1b16	1.0566	0.036432
Klk1b24	1.054724	0.036449
Tspan18	0.957284	0.038389
Cd300e	1.033356	0.038389
Fgf21	1.007764	0.039701
Maf	0.966742	0.040167
Fcrls	0.963404	0.04046
Plcb1	0.774824	0.040519
Nlrp1b	0.967911	0.040654
Ceacam18	0.869294	0.04151

Gene Symbol	Log2 fold change	Adjusted p value
Klk1b27	0.993791	0.04151
Hbegf	0.874976	0.04153
Sulf2	0.914505	0.04153
Il18	1.008716	0.044145
Iqgap3	0.643173	0.045413
Trim72	1.02456	0.045766
Ssxb1	1.002203	0.047744
Gm16897	0.797845	0.047927
Trim30d	0.814938	0.04873
Nlrp1a	0.834254	0.049001
Insl6	0.914627	0.049001
Ccr12	0.921196	0.049497

Table S5. Related to Figure 5. Differentially regulated genes (fold> 1.5, p<0.05), between Jmjd1c^{ff} and Jmjd1c^{-/-} Hoxa9/Meis1 leukemic cells

Gene Symbol	Log2 fold change	Adjusted p value
Pcdh7	-0.6696	3.31E-11
Plekhh2	-0.7997	1.63E-09
Eltd1	-1.09429	5.80E-08
Armcx4	-0.86084	3.45E-06
Cth	-1.0242	5.21E-06
Zcchc14	-1.0095	7.28E-06
Fam174b	-0.7281	7.22E-05
Aldh1l2	-0.86677	0.000155
Gm12709	-0.68523	0.000297
Pcdhgc3	-0.59696	0.00035
Glyat	-0.70295	0.000444
Rgs8	-0.80111	0.000461
Mir17hg	-0.59387	0.001125
Sgip1	-0.58538	0.002367
Kdelc2	-0.59198	0.002579
Prrg4	-0.61959	0.002646
Ggact	-0.69016	0.003254
Slc6a9	-0.72075	0.004488
Sacs	-0.65441	0.005365
Ccdc40	-0.61917	0.006351
Hid1	-0.69969	0.006586
Pitpnm2	-0.65972	0.007643
Cdr2l	-0.69309	0.007799
Ctnna2	-0.6323	0.007861
Col5a3	-0.60123	0.008672
Nr0b2	-0.59415	0.010108
Six4	-0.66491	0.010717
Hmgn3	-0.63107	0.011606
Cpeb1	-0.62029	0.011814
Extl1	-0.64644	0.015151
Aldh1a3	-0.63391	0.019066
B130034C11Rik	-0.62497	0.01942

Gene Symbol	Log2 fold change	Adjusted p value
4930565N06Rik	-0.58678	0.024453
Tacc2	-0.61591	0.024672
Tfr2	-0.61115	0.028009
Pcsk9	-0.59344	0.030253
Msantd3	-0.59049	0.030521
Spry4	-0.59693	0.032571
Dab2	1.577363	2.88E-25
Wfdc17	1.769478	5.22E-24
Cd74	2.111213	1.15E-22
Rgl1	1.360868	1.74E-21
Tlr7	1.511707	7.86E-21
Itgb3	1.144434	2.75E-19
Tsc22d1	1.110369	4.09E-19
Ndrp1	0.738532	1.54E-18
C1qb	1.893992	1.74E-18
Msr1	1.850818	2.83E-18
Fyb	1.519498	3.24E-18
Gpnmb	1.496143	5.12E-18
Sdc3	1.181379	2.25E-17
Pira1	1.534865	2.20E-16
Gm14548	1.529021	9.56E-16
Hmox1	1.125987	9.94E-16
Pira11	1.517736	1.87E-15
Pira6	1.521911	1.89E-15
Bank1	1.528635	3.40E-15
Abca1	1.758163	5.22E-15
C3ar1	1.685126	8.28E-43
Ctss	1.354344	4.70E-40
Pira4	1.454763	9.88E-31
Pira7	1.454357	5.37E-27
Fos	1.405475	1.77E-26
Al607873	1.681568	4.49E-26

Gene Symbol	Log2 fold change	Adjusted p value
Rara	0.914205	5.51E-15
Tgfb1	1.551244	1.01E-14
Stk17b	1.019443	2.57E-14
Ahnak	1.454799	5.89E-14
Rap1gap2	1.221421	8.44E-14
Gas7	1.168082	2.66E-13
Hlx	0.755542	2.70E-13
C1qc	1.586292	3.86E-13
Sema4d	0.621361	3.86E-13
Plek	1.112969	3.99E-13
Arl4c	1.120821	4.36E-13
Abcg1	0.823972	4.42E-13
Ifi204	1.572883	4.48E-13
C1qa	1.570706	9.27E-13
Ptpro	1.513429	9.91E-13
Ccl3	0.966588	9.92E-13
Ifi2712a	0.906601	1.22E-12
Lgm1	1.45207	1.32E-12
Chn2	0.768674	1.37E-12
Slfn5	1.067639	2.66E-12
Fosl2	0.916529	2.94E-12
Id2	1.110961	5.77E-12
Zfp36	0.991843	6.12E-12
Mir5107	1.510752	6.49E-12
Lpl	1.337098	6.49E-12
Marcks	1.486582	1.20E-11
Trem2	1.457636	1.51E-11
Gapt	0.917488	1.55E-11
Fcgr1	1.475111	2.12E-11
Mpeg1	1.044586	2.56E-11
Map3k8	1.004635	2.74E-11
Spint1	1.437058	7.82E-11

Gene Symbol	Log2 fold change	Adjusted p value
Itgb5	0.74976	1.60E-10
Abi3	1.003172	1.66E-10
Maf	1.379523	2.00E-10
Pira2	1.273463	2.60E-10
Olfm1	1.380383	3.63E-10
Oas3	0.624387	6.84E-10
Ifit1	1.158213	9.33E-10
Tpd52	0.595469	1.09E-09
Ms4a4c	1.361147	1.19E-09
Lrrc32	0.915122	1.45E-09
Nlrp3	0.843923	1.52E-09
Cd80	1.268676	2.29E-09
Adora2b	0.769775	2.29E-09
Asph	0.724281	2.34E-09
Il10ra	0.782412	4.14E-09
Sh2d3c	0.962513	5.87E-09
Slc15a3	1.286837	7.76E-09
Cd200r4	0.897327	9.81E-09
Lgals3	0.884147	9.81E-09
Ier5	0.910574	1.02E-08
Abcg3	1.135904	1.13E-08
Clec4a3	1.291531	1.20E-08
Jun	0.915925	1.23E-08
Htra3	1.278086	1.33E-08
Psap	0.829862	1.40E-08
P2ry13	1.286848	1.40E-08
Ptgs2	1.230081	1.52E-08
Rcbtb2	0.752929	1.60E-08
Xdh	1.035627	1.67E-08
Ptafr	1.141942	2.08E-08
Mmp12	1.027811	2.37E-08
Mtss1	0.613567	2.45E-08

Gene Symbol	Log2 fold change	Adjusted p value
Ddx60	0.875422	1.10E-06
Atp7a	0.829088	1.35E-06
Hpse	0.610433	1.45E-06
AF251705	0.943269	1.52E-06
Dusp5	0.612887	1.53E-06
Krt80	1.046971	1.63E-06
Egr2	1.117191	1.67E-06
Egr1	0.968637	1.73E-06
Tnfaip3	0.798601	1.85E-06
Plxdc2	1.102674	2.00E-06
Stk10	0.648879	2.13E-06
Ccr5	1.053921	2.63E-06
Galnt6	0.666531	2.63E-06
Gm5431	1.095884	2.67E-06
Nrp1	0.837058	2.83E-06
Zbp1	0.650097	3.08E-06
Btg1	0.672827	3.14E-06
Csf1	0.835166	3.69E-06
Il6ra	0.933695	3.87E-06
Rasgrp4	0.707174	4.00E-06
Neur13	0.73757	4.12E-06
Ndst1	0.665892	4.60E-06
Klf2	0.634919	5.04E-06
Myof	1.065667	5.23E-06
Trim30d	0.691385	5.27E-06
Slc2a3	0.835288	5.70E-06
Map3k5	0.633284	6.57E-06
Phospho1	0.955146	7.89E-06
Rbms1	0.832828	7.89E-06
B430306N03Rik	0.878714	7.99E-06
Stx3	1.008231	9.04E-06
Lyn	0.618026	1.02E-05

Gene Symbol	Log2 fold change	Adjusted p value
Serpinb2	1.031839	1.11E-05
Slfn2	0.738181	1.16E-05
Nt5e	0.929323	1.36E-05
Klf6	0.765379	1.45E-05
Mitf	0.683657	1.48E-05
Cd36	1.005925	1.54E-05
Sfxn5	0.940947	1.54E-05
Tnfrsf9	0.921182	1.58E-05
Zc3h12d	0.982046	1.81E-05
Dse	0.748395	1.90E-05
Ifit3	0.983564	2.95E-05
Vcan	0.874651	3.02E-05
Cd9	0.836215	3.12E-05
H2-DMb2	0.870872	3.27E-05
Emp1	0.991584	3.54E-05
Oit3	0.963087	3.54E-05
Lilra6	0.989432	3.66E-05
Nos2	0.959185	3.84E-05
9130019P16Rik	0.674831	4.41E-05
Evi2a	0.614136	4.67E-05
Wipi1	0.61696	4.74E-05
Sgms1	0.859832	5.12E-05
AA467197	0.912963	5.14E-05
Ahr	0.951963	5.32E-05
Gbp9	0.77578	5.41E-05
Plaur	0.797259	5.53E-05
Pydc4	0.954931	5.57E-05
Siglec1	0.96348	6.56E-05
Ankrd33b	0.953066	7.71E-05
Lif	0.820162	8.01E-05
Clvs1	0.641664	8.17E-05
Tlr5	0.931782	8.89E-05

Gene Symbol	Log2 fold change	Adjusted p value
Bcl2l11	0.599555	8.99E-05
Zfhx3	0.799855	9.26E-05
Ifnlr1	0.923373	0.000107
Osgin1	0.755226	0.000108
Gcnt2	0.907464	0.000115
Hgf	0.717698	0.000116
Gsn	0.912154	0.000126
Cox4i2	0.862013	0.000134
Trim30b	0.914968	0.000143
Pik3r6	0.604379	0.00016
Dusp1	0.792161	0.000174
Ms4a6c	0.762204	0.000181
Gm10684	0.83097	0.000186
Tnip3	0.909384	0.000189
Cd52	0.631994	0.00019
P2ry6	0.845421	0.000218
4632428N05Rik	0.700703	0.000223
Adora3	0.895125	0.000228
Upp1	0.900904	0.000243
Mylk	0.641149	0.000245
Ly6g5b	0.818503	0.000255
Samhd1	0.637422	0.000255
P2ry14	0.846147	0.000258
Cd300ld	0.744182	0.000312
Fam129a	0.815761	0.000323
Arhgef3	0.659321	0.000324
Grina	0.608174	0.000324
Csf1r	0.879604	0.000333
Pirb	0.877612	0.000341
Zcwpw1	0.737607	0.000375
Fam49a	0.730829	0.000375
Pik3r5	0.695478	0.000379

Gene Symbol	Log2 fold change	Adjusted p value
Klk1b9	0.830553	0.000383
Tlr8	0.823616	0.000389
Card6	0.855439	0.000399
Cd38	0.865533	0.000402
Tgm3	0.843185	0.000405
Hbegf	0.686427	0.000409
Arg2	0.869027	0.000413
P2rx7	0.827933	0.000417
Susd3	0.684238	0.000422
Tagap	0.72946	0.000422
Ccl2	0.864609	0.000445
Tgfbr2	0.607328	0.000468
Havcr2	0.860498	0.000511
Serpib10	0.841698	0.00052
Anxa1	0.84248	0.000556
LOC100038947	0.792733	0.000603
Anxa11	0.636236	0.000612
Mnda	0.790576	0.000627
Adam8	0.831662	0.000636
Card10	0.809776	0.000693
Lsp1	0.832522	0.000766
Cdc42ep2	0.839408	0.000794
Nfkbiz	0.676921	0.000883
Mir147	0.803633	0.000886
Tesc	0.698141	0.000899
Cnr2	0.680933	0.000904
Spatc1	0.823865	0.000921
0610040F04Rik	0.679999	0.000945
Dfna5	0.642989	0.000965
Pag1	0.602187	0.000995
Pgf	0.805878	0.001054
Smpd5	0.641201	0.001093

Gene Symbol	Log2 fold change	Adjusted p value
Rassf4	0.58827	0.001095
Zmat3	0.608775	0.001128
Rab37	0.724788	0.001194
AI839979	0.702629	0.001307
Ublcp1	0.762329	0.001308
Gpr55	0.775807	0.001493
Serpina3f	0.647839	0.00152
Clec7a	0.718782	0.001534
Gm17455	0.705232	0.001542
Epb4.1l1	0.734961	0.001597
Mertk	0.753363	0.001597
Slc37a2	0.706546	0.001687
Klra2	0.782252	0.001703
Usp18	0.635214	0.001703
Gbp4	0.610375	0.001703
Tulp4	0.723561	0.001703
Tnfrsf23	0.777344	0.001735
Lyz2	0.790456	0.001772
Bcl2a1b	0.769015	0.001795
Gp49a	0.788542	0.00181
Prr33	0.788434	0.001848
Scel	0.771557	0.001848
Tnfsf12	0.601574	0.001949
Rnase6	0.729289	0.002005
Bmf	0.653051	0.00201
Itpr2	0.702875	0.002047
Il1r2	0.767484	0.002049
Saa3	0.773761	0.002112
Il1b	0.727959	0.002147
Galnt9	0.679926	0.002147
Nov	0.725157	0.002193
Cpeb2	0.601672	0.002193

Gene Symbol	Log2 fold change	Adjusted p value
Cd101	0.767077	0.002195
Pf4	0.77002	0.002206
Sulf2	0.734517	0.002367
Nedd9	0.644775	0.002371
Ptms	0.746152	0.002522
Myo1e	0.619113	0.002595
Mctp1	0.643768	0.002597
5031414D18Rik	0.631982	0.002617
Aif1	0.73089	0.002727
Atf3	0.632308	0.003009
Dpep3	0.735727	0.003019
Sirpb1b	0.662065	0.003183
Kcne3	0.63974	0.003233
Zfp36l1	0.750779	0.00361
Wfdc18	0.670318	0.003945
Rnf150	0.740399	0.004256
Arg1	0.735609	0.00451
Nos1ap	0.638483	0.004561
Tmcc3	0.665225	0.004647
Ly6a	0.655151	0.00469
Nrg1	0.606831	0.005126
Adora2a	0.690538	0.005162
Irgc1	0.643986	0.005186
Scn1b	0.72599	0.005307
Ceacam1	0.601987	0.005353
Antxr2	0.674379	0.005389
Gpr35	0.639155	0.005498
Ccdc80	0.699847	0.005505
Clec4n	0.643169	0.005754
1-Mar	0.63175	0.005754
Bcl2a1d	0.661164	0.005794
Cd300lf	0.698372	0.005859

Gene Symbol	Log2 fold change	Adjusted p value
Slc7a8	0.62331	0.006001
Lifr	0.710515	0.006253
Cd300c	0.713449	0.0063
2010002M12Rik	0.701788	0.006308
Abtb2	0.705477	0.006548
Grk5	0.700011	0.006598
Ppp1r3d	0.672786	0.006692
Rhov	0.707924	0.006786
Axl	0.676	0.006836
Il12rb2	0.644753	0.007331
Plk2	0.70369	0.007514
Gm9733	0.674002	0.00759
Klk1b11	0.595797	0.007643
H2-Eb1	0.698122	0.007892
Slc44a1	0.645027	0.008623
Dhrs9	0.640046	0.008623
Epm2a	0.684668	0.008805
Fas	0.664474	0.009115
Phlda1	0.682851	0.009176
Scrg1	0.587021	0.010496
H2-Aa	0.656786	0.010525
Ctse	0.664618	0.010608
Hck	0.650795	0.010901
Sycp2	0.64836	0.010972
Mir6367	0.63609	0.010972
Reps2	0.6704	0.011046
Fcnb	0.617039	0.011287
Tlr13	0.631369	0.011513
Bcl2a1a	0.665986	0.011526
Gm6377	0.631249	0.011594
Klk1b1	0.586761	0.011993
Cyp4f18	0.636987	0.014663
Gas6	0.624403	0.015064

Gene Symbol	Log2 fold change	Adjusted p value
Camk1d	0.649447	0.015106
Tnfsf8	0.616739	0.015415
Il18r1	0.653057	0.01543
Ipcef1	0.628712	0.01683
8430408G22Rik	0.587319	0.017749
Creb5	0.642759	0.018265
C330046G13Rik	0.630282	0.018616
Rragd	0.598578	0.018629
6330409D20Rik	0.64025	0.018636
Col1a1	0.625884	0.019122
Il27	0.628733	0.019305
C130026I21Rik	0.609898	0.019409
Plxna1	0.598917	0.020318
4921529L05Rik	0.629269	0.021926
Clec4b2	0.599473	0.021926
Kcnk13	0.621593	0.022167
Inhba	0.614645	0.022502
Rasgrp1	0.625614	0.023473
Arl5c	0.623164	0.024138
Car2	0.588285	0.025369
Ltb	0.596316	0.026545
A630033H20Rik	0.587179	0.027667
Pilrb1	0.603611	0.027711
Trp53inp1	0.602943	0.027742
Ppp1r16b	0.609004	0.028826
Lpcat2	0.589851	0.028831
Mir1903	0.606762	0.029352
Grap2	0.604711	0.029955
Pik3c2b	0.597985	0.032227
Tg	0.592525	0.034157
Map3k9	0.591281	0.035636
Mxd1	0.590848	0.035767
Gm1673	0.590311	0.036027

Jmjd1c ranks #14 in all down-regulated genes with Log2 fold change of -0.50105 and adjusted p value of 3.86E-05.

Table S6. Related to Figure 7. Differentially regulated genes (fold> 1.5, p<0.05) in LSK cells between Vav1Cre and Jmjd1c^{fl}:Vav1Cre mice

Gene Symbol	Log2 fold change	Adjusted p value
Wdfy1	-1.07858	1.03E-13
Ly6c2	-0.79307	1.39E-11
Jmjd1c	-0.88782	3.22E-09
Gm15446	-1.7521	4.00E-06
Fn1	-1.10458	0.000337
Fcnb	-0.61544	0.003096
Ighg2c	-5.17506	0.009648
Clec12a	-0.75467	0.011214
Gimap4	-1.07387	0.016526
Rnase4	-1.03881	0.016917
Il7r	-0.95276	0.020307
Ccl3	-1.12332	0.020804
Hepacam2	-1.54391	0.030904
Ighv1-26	-3.79986	0.036573
F13a1	-0.6388	0.047106
Chtf8	0.931736	3.76E-06
Prep	0.798554	1.65E-05
Ints1	0.944328	1.92E-05
Ppif	0.608105	6.43E-05
Ncdn	0.84471	0.000337
Igfbp4	0.675156	0.000715
Sf3b4	0.683951	0.000722
Clnk	0.866248	0.000722
Cad	0.679825	0.000801
Cd276	1.501615	0.001992
Atf6b	0.743831	0.00232
Ppa2	0.819458	0.00236
Mri1	1.342676	0.003544
Srrt	0.659789	0.004194
Nop9	0.789621	0.004417
Med16	0.667674	0.009648
Gtdc2	-0.8075	0.01841

Gene Symbol	Log2 fold change	Adjusted p value
Ptk7	1.051968	0.010065
Tcof1	0.585742	0.011972
Rae1	0.596786	0.012259
Lmnb2	0.709808	0.01315
Tcf3	0.855338	0.016526
BC030867	0.615055	0.017827
Runx3	0.670999	0.017827
Igkv4-91	2.898587	0.017827
Sumf1	1.114823	0.018828
Eif3b	0.665685	0.020023
Zfp553	0.701895	0.020023
Cdc20	0.657642	0.020804
Ubap2	0.665521	0.020804
Prpsap1	1.022591	0.020804
Pkmyt1	0.953077	0.022384
Emid1	1.543813	0.022606
Arhgef1	0.629735	0.024376
Il12rb1	0.998032	0.024376
Vars	0.779237	0.02515
Sf1	0.643128	0.025498
Eif2b5	1.136263	0.025498
Padi4	0.926041	0.030017
Znhit2	1.268875	0.030017
Tbc1d9b	0.709311	0.030904
Ttyh2	0.742959	0.030904
Impdh1	0.845092	0.031644
Vps37b	0.650417	0.03261
Cdk9	0.835503	0.034626
U2af2	0.632322	0.036573
Phrf1	0.668619	0.036573
Cpne2	0.788692	0.043173
Polr2a	0.654853	0.043543

Gene Symbol	Log2 fold change	Adjusted p value
Mybl2	0.807813	0.043728
Itga2b	0.608822	0.047106
Med30	1.856448	0.047355
Mgat2	0.639051	0.04848
Pola2	0.692278	0.04923