Supplementary Data

Supplementary Figure 1: Frameshift deletions in *SETD2* and *MSH6* in MOLM-13 subclones

Supplementary Figure 2: Chromatin Immunoprecipitation-Sequencing with Drosophila chromatin spike in normalization

Supplementary Figure 3: *In vitro* cytarabine resistance for murine MLL-AF9 cells

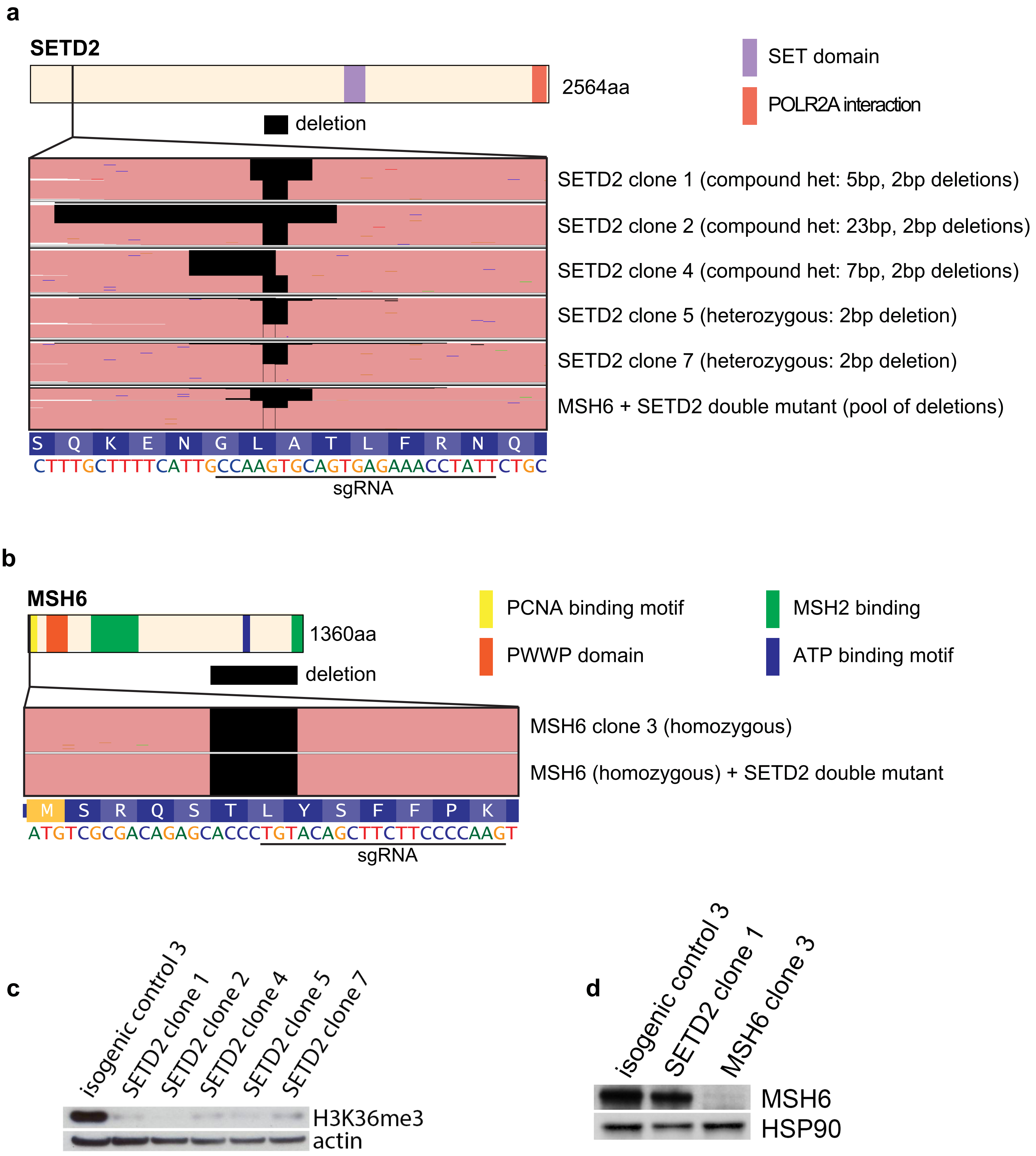
Supplementary Figure 4: *SETD2* loss and impairment of MSH6 localization

Supplementary Figure 5: Additional studies of MLL-AF9 Setd2 mutant leukemia

Supplementary Table 1: *SETD2* mutations reported in Pediatric Acute Lymphoblastic Leukemia and Hematological Malignancies in the Catalog of Somatic Mutations in Cancer (COSMIC)

Supplementary Table 2: Small guide sequences and primers used

Supplementary Table 3: Novel clonal mutations identified in 6-thioguanine treated MOLM-13 subclones

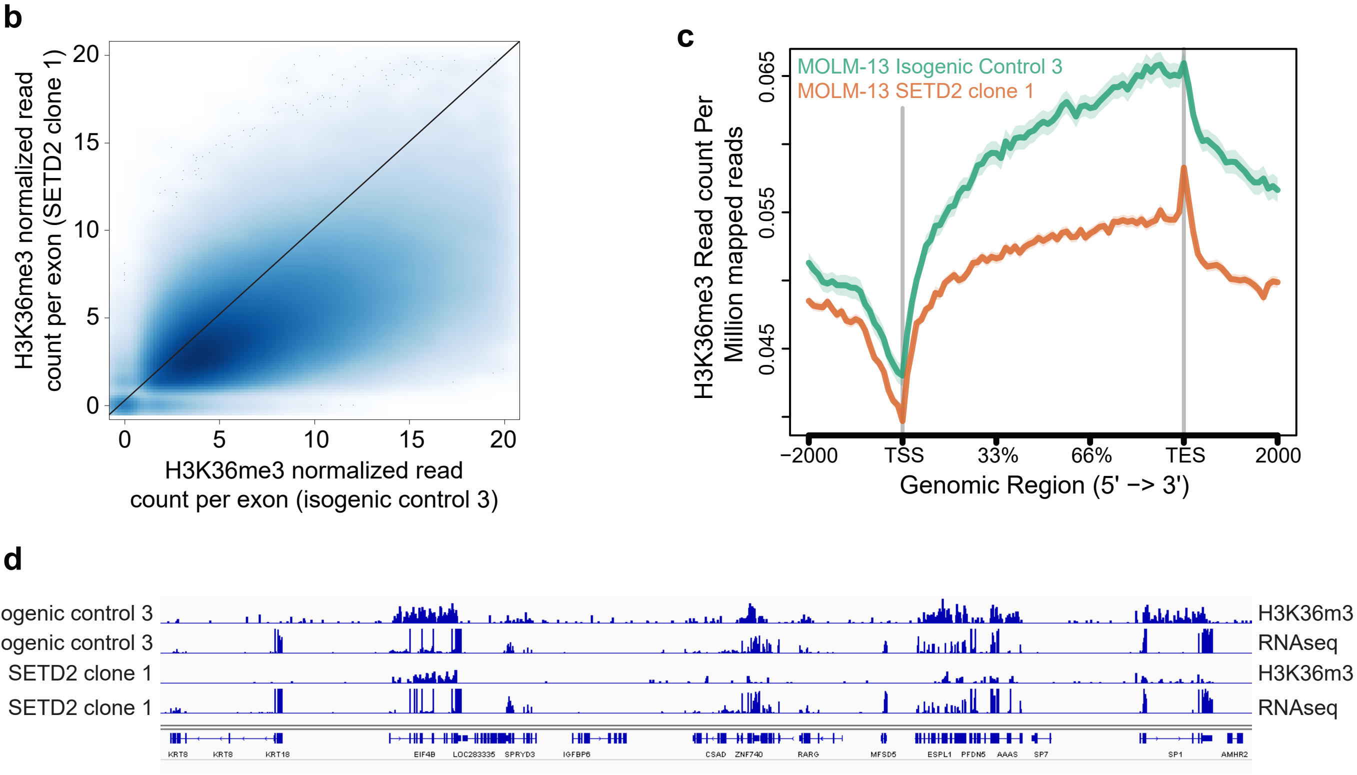


Supplementary Figure 1. Frameshift deletions in *SETD2* and *MSH6* in MOLM-13 sub-clones. a) Genomic DNA was PCR amplified and next generation sequencing was used to quantitatively determine the presence of deletions in each clone. Each schematic shows the location of the sgRNA in relationship to the *SETD2* or **b)** *MSH6* protein and its known domains, and shows the relavent aligned reads with deletions in black. Colors other than pink represent mismatches in the alignment, some of which may represent reads with large insertions or deletions that misaligned to the genome. **c)** Western blot for H3K36me3 of MOLM-13 subclones with *SETD2* deletions and isogenic control 3. **d)** Western blot for MSH6 of MOLM-13 subclones with *MSH6* deletions and isogenic controls.

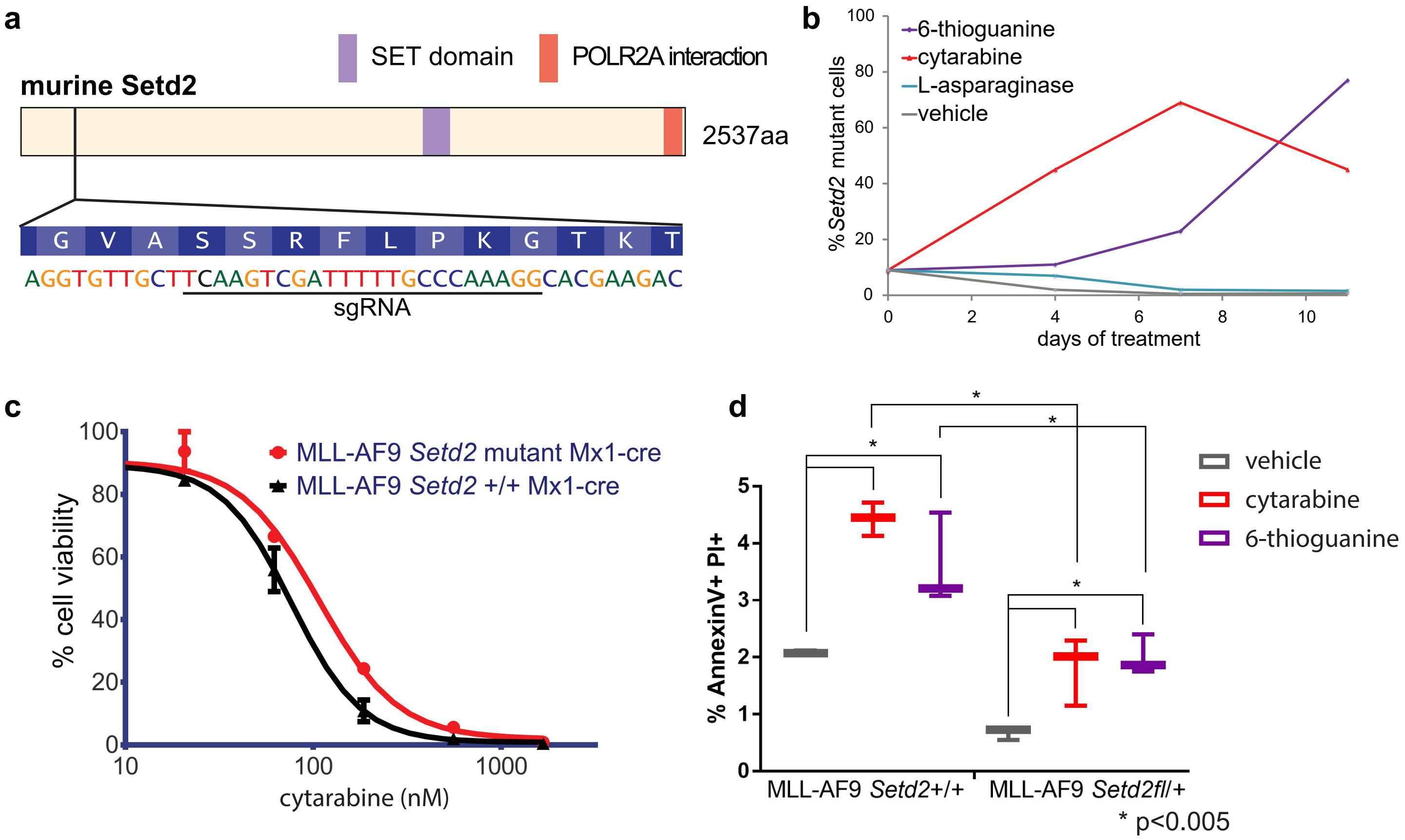
a

Sample	Histone Mark	Dm ReadCountTotal	Hg ReadCountTotal	SpikeIn_Norm	Depth_Norm*
MOLM-13 isogenic control 3	H3K36me3	656,423.00	40,158,309.00	1.523	0.249
MOLM-13 SETD2 clone 1	H3K36me3	786,053.00	37,474,822.00	1.272	0.267

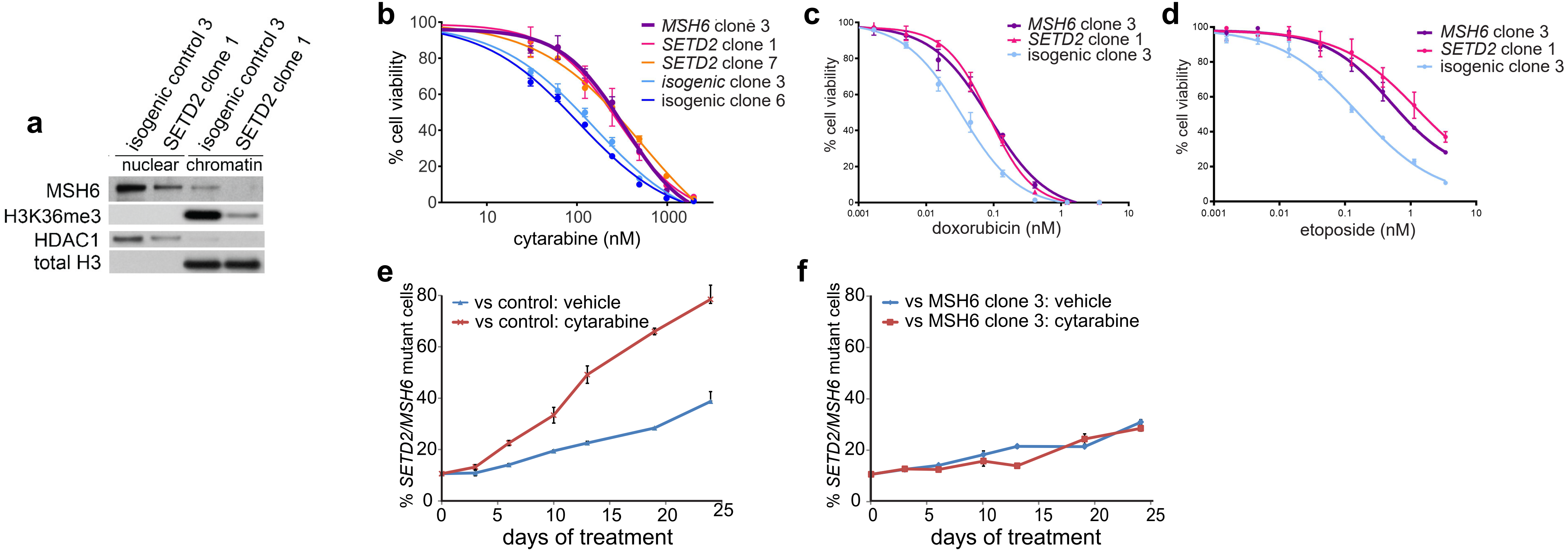
*Normalized to 10 million reads



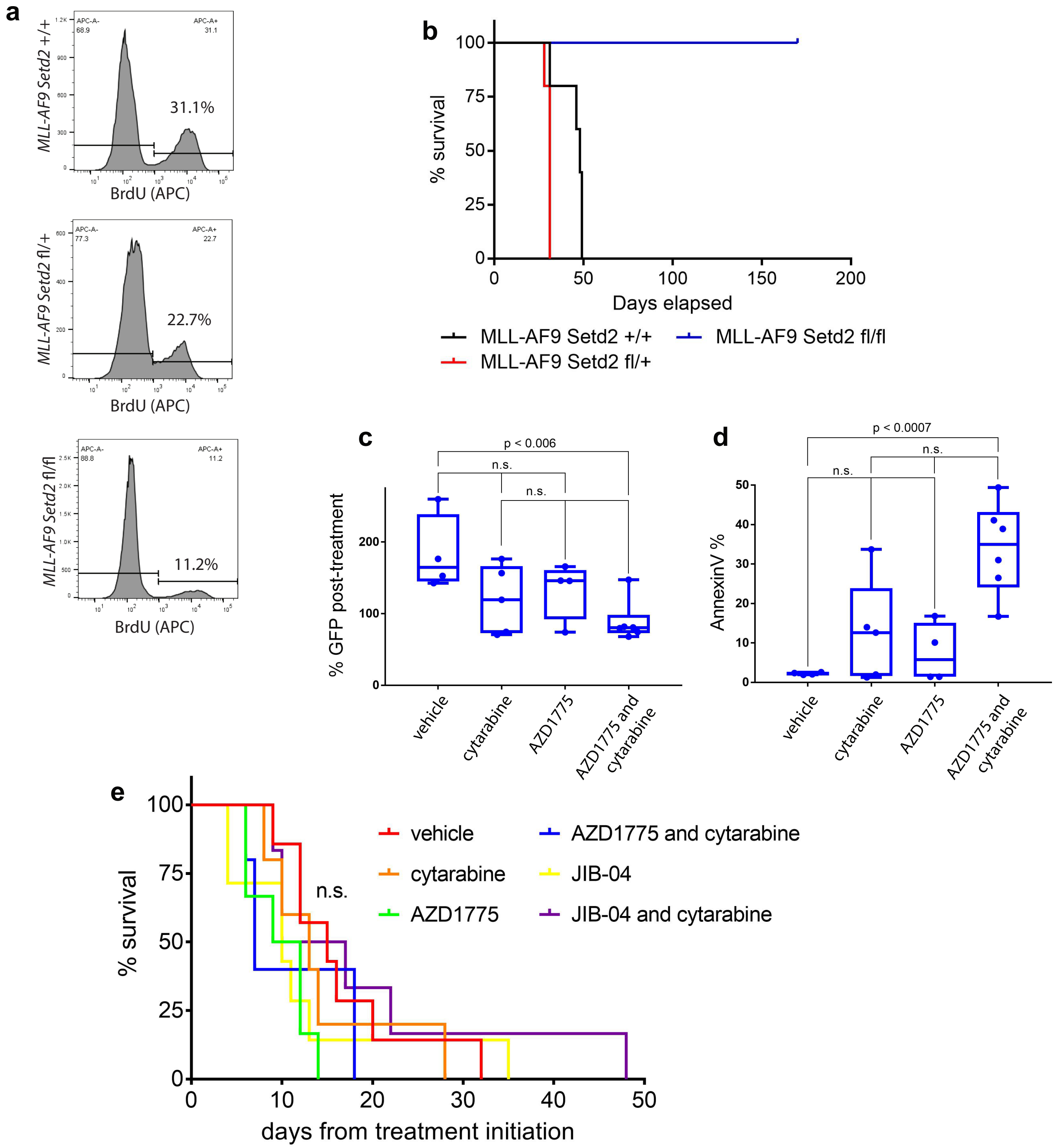
Supplementary Figure 2. Chromatin Immunoprecipitation-Sequencing with Drosophila chromatin spike in normalization. a) Sequencing metrics with normalization factors used. **b)** H3K36me3 chromatin immunoprecipitation sequencing reads, normalized to Drosophila chromatin spike-in, for expressed and non-expressed genes, normalized for gene body length, in MOLM-13 subclones with a *SETD2* sgRNA (*SETD2* clone 1) or isogenic control 3. Gene expression was determined by RNA sequencing. TSS = Transcriptional Start Site, TES = Transcriptional End Site. **c)** H3K36me3 levels over all genes, normalized over gene body length between the vertical lines. TSS: Transcriptional Start Site. TES: Transcriptional End Site. **d)** Representative view of normalized H3K36me3 and expression at the gene level in the Integrated Genome Viewer.



Supplementary Figure 3. In vitro cytarabine resistance of murine *MLL-AF9 Setd2* mutated cells. a) CRISPR/Cas9 was used to induce frameshift mutations in the exon 3 of *Setd2* in murine *MLL-AF9* cells. Schematic shows the location and sequence of the sgRNA targeting *Setd2*. **b)** Murine MLL-AF9 cells was transduced with a lentivirus Cas9-puro and selected with puro, then transduced with a lentivirus expressing a sgRNA to *Setd2* and RFP657. This was mixed with *MLL-AF9* Cas9-puro cells in a 1:10 ratio and then treated with cytarabine, 6-thioguanine, L-asparaginase or vehicle. In this pooled experiment, in the absence of selective pressure of 6-thioguanine or cytarabine, sgRNA editing of *Setd2* likely goes to completion, which may explain de-enrichment in the vehicle and L-asparaginase arms. **c)** Conditional knockout *MLL-AF9 Setd2* mutant and *Setd2+/+* cells were assessed for *in vitro* chemotherapy resistance. Cell titer Glo was used to determine % cell viability after 72 hours of cytarabine. **d)** *MLL-AF9 Setd2* mutant and *Setd2+/+* cells were treated with cytarabine 50nM, or 6-thioguanine 50nM and assessed for apoptosis by flow cytometry after staining for AnnexinV and propridium iodide 24 hours later.



Supplementary Figure 4. SETD2 loss, impairment of MSH6 localization and MSH6 loss induced chemotherapy resistance. **a)** MOLM-13 SETD2 clone 1 and MOLM-13 isogenic control 3 cells were fractionated into nuclear or chromatin compartments and Western blotted. HDAC1 and total H3 are the loading controls for the nuclear and chromatin fractions, respectively. **b)** Cell titer Glo was used to determine % cell viability after 72 hours of araC, **c)** doxorubicin or **d)** etoposide treatment for MOLM-13 MSH6 clone 3, SETD2 clones and isogenic controls. MOLM-13 MSH6 clone 3 was transduced with a Cas9-SETD2 sgRNA and then an RFP+ lentivirus. This was mixed with **e)** isogenic control 3 or **f)** MSH6 clone 3 in a 1:10 ratio and treated with araC or vehicle for 25 days and followed by flow cytometry for tdTomato.



Supplementary Figure 5. Additional studies of *MLL-AF9 Setd2* mutant leukemia
a) BrdU cell cycle analysis of primary *MLL-AF9* leukemia cells grown *in vitro*. **b)** 50,000 bone marrow cells from mice (n=5 in each arm) with primary MLL-AF9 *Setd2 +/+*, *Setd2 fl/+* or *Setd2 fl/fl* Mx1-cre leukemia were injected into secondary C57BL/6 recipients and monitored for the development of leukemia and sacrificed when moribund. **c)** Mice with secondary MLL-AF9 Setd2fl/+ Mx1-cre leukemia received a single dose of vehicle (n=4), araC (n=5), AZD1775 (n=4) and araC with AZD1775 (n=6) when their peripheral blood GFP was approximately 40% and were re-bled 12-16 hours later to determine the reduction in cell number, expressed as a percent of pre-treatment GFP, or **d)** stained with AnnexinV to determine the amount of apoptosis following treatment. **e)** Mice with secondary MLL-AF9 Setd2fl/+ Mx1-cre leukemia initiated treatment with 5 days of or vehicle (n=7), cytarabine (n=5), AZD1775 (n=6), AZD1775 and cytarabine (n=5), JIB-04 (n=7), JIB-04 and cytarabine (n=6 when peripheral blood GFP was around 5%.

Supplementary Table 1: *SETD2* mutations reported in Pediatric Acute Lymphoblastic Leukemia and Hematological Malignancies in the Catalog of Somatic Mutations in Cancer (COSMIC)

DFCI Pediatric B-ALL cohort

Sample	specimen	Genome pos.	Gene	Isoform	Mutation	Ref	Alt	LOH	Pubmed ID	diagnosis_full	diagnosis_subtype	Class
TCALL015	DIAGNOSIS	chr3:47129621	SETD2	NM_014159	p.T1753fs	AC	-	Yes	24662245	B-cell Acute Lymphoblastic Leukemia		FRAMESHIFT
TCALL027	DIAGNOSIS	chr3:47164571	SETD2	NM_014159	p.K519_R520delinsX	A	-	No	24662245	B-cell Acute Lymphoblastic Leukemia	hyperdiploidy	NONSENSE
TCALL056	DIAGNOSIS	chr3:47058642	SETD2	NM_014159	p.K2546X	A	T	Yes	24662245	B-cell Acute Lymphoblastic Leukemia		NONSENSE
TCALL027	RELAPSE	chr3:47164571	SETD2	NM_014159	p.K519_R520delinsX	A	-	No	24662245	B-cell Acute Lymphoblastic Leukemia	hyperdiploidy	NONSENSE
TCALL037	RELAPSE	chr3:47144908	SETD2	NM_014159	p.I1615fs	A	-	No	24662245	B-cell Acute Lymphoblastic Leukemia	iAMP21	FRAMESHIFT
TCALL056	RELAPSE	chr3:47058642	SETD2	NM_014159	p.K2546X	A	T	Yes	24662245	B-cell Acute Lymphoblastic Leukemia		NONSENSE
ASALL011	DIAGNOSIS	chr3:47162032	SETD2	NM_014159	p.G1365E	C	T	No	24662245	B-cell Acute Lymphoblastic Leukemia	hyperdiploidy	MISSENSE
ASALL028	DIAGNOSIS	chr3:47125808	SETD2	NM_014159	p.L1821P	A	G	No	24662245	B-cell Acute Lymphoblastic Leukemia		MISSENSE
ASALL033	DIAGNOSIS	chr3:47125526	SETD2	NM_014159	p.V1915A	A	G	No	24662245	B-cell Acute Lymphoblastic Leukemia	hyperdiploidy	MISSENSE
ASALL039	DIAGNOSIS	chr3:47165327	SETD2	NM_014159	p.V267I	C	T	No	24662245	B-cell Acute Lymphoblastic Leukemia	ETV6/RUNX1	MISSENSE
ASALL043	DIAGNOSIS	chr3:47161880	SETD2	NM_014159	p.E1416X	C	A	No	24662245	B-cell Acute Lymphoblastic Leukemia	MLL rearrangement	NONSENSE
ASALL044	DIAGNOSIS	chr3:47163744	SETD2	NM_014159	p.Y794X	G	C	No	24662245	B-cell Acute Lymphoblastic Leukemia		NONSENSE
ASALL048	DIAGNOSIS	chr3:47142975	SETD2	NM_014159	p.T1663M	G	A	No	24662245	B-cell Acute Lymphoblastic Leukemia		MISSENSE
ASALL050	DIAGNOSIS	chr3:47162615	SETD2	NM_014159	p.T1171A	T	C	No	24662245	B-cell Acute Lymphoblastic Leukemia	hyperdiploidy	MISSENSE
ASALL077	DIAGNOSIS	chr3:47161769	SETD2	NM_014159	p.D1453N	C	T	No	24662245	B-cell Acute Lymphoblastic Leukemia		MISSENSE
ASALL078	DIAGNOSIS	chr3:47205410	SETD2	NM_014159	p.K2R	T	C	No	24662245	B-cell Acute Lymphoblastic Leukemia	BCR-ABL	MISSENSE
ASALL079	DIAGNOSIS	chr3:47162777	SETD2	NM_014159	p.F1117fs	A	-	No	24662245	B-cell Acute Lymphoblastic Leukemia	ETV6/RUNX1	FRAMESHIFT
ASALL080	DIAGNOSIS	chr3:47164718	SETD2	NM_014159	p.S470P	A	G	No	24662245	B-cell Acute Lymphoblastic Leukemia		MISSENSE
ASALL108	DIAGNOSIS	chr3:47205359	SETD2	NM_014159	p.E19G	T	C	No	24662245	B-cell Acute Lymphoblastic Leukemia	MLL rearrangement	MISSENSE
ASALL111	DIAGNOSIS	chr3:47164571	SETD2	NM_014159	p.K519R520delinsX	-	T	No	24662245	B-cell Acute Lymphoblastic Leukemia	hyperdiploidy	NONSENSE
ASALL115	DIAGNOSIS	chr3:47205410	SETD2	NM_014159	p.K2R	T	C	No	24662245	B-cell Acute Lymphoblastic Leukemia		MISSENSE
ASALL119	DIAGNOSIS	chr3:47162900	SETD2	NM_014159	p.S1076P	A	G	No	24662245	B-cell Acute Lymphoblastic Leukemia	ETV6/RUNX1	MISSENSE

SJCRH Pediatric ALL Cohort

Sample	specimen	Genome pos.	Gene	Isoform	Mutation	Ref	Alt	LOH	Pubmed ID	diagnosis	diagnosis_subtype	Class
SJERG005_D	DIAGNOSIS	chr3:47129620	SETD2	NM_014159	C1754R	A	G	No	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJTALL199_D	DIAGNOSIS	chr3:47164805	SETD2	NM_014159	R441*	G	A	Not available	22237106	T-cell Acute Lymphoblastic Leukemia	ETP	NONSENSE
SJTALL173_D	DIAGNOSIS	chr3:47155452	SETD2	NM_014159	P1534_R1543fs	CCGTCTATTGGAACAATAATCCCCATTT	-	Not available	22237106	T-cell Acute Lymphoblastic Leukemia	ETP	FRAMESHIFT
SJTALL202_D	DIAGNOSIS	chr3:47125363	SETD2	NM_014159	K1969fs	-	CT	Not available	22237106	T-cell Acute Lymphoblastic Leukemia	ETP	FRAMESHIFT
SJTALL202_D	DIAGNOSIS	chr3:47164508	SETD2	NM_014159	R540*	G	A	Not available	22237106	T-cell Acute Lymphoblastic Leukemia	ETP	NONSENSE
SJTALL190_D	DIAGNOSIS	chr3:47162558	SETD2	NM_014159	V1190M	C	T	Not available	24710217	T-cell Acute Lymphoblastic Leukemia	ETP	MISSENSE
SJBALL021373_D1	DIAGNOSIS	chr3:47139530	SETD2	NM_014159	R1686P	C	G	Not available	25207766	B-cell Acute Lymphoblastic Leukemia	iAmp21 ALL	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47162371	SETD2	NM_014159	S1252*	G	T	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	NONSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47162642	SETD2	NM_014159	H1162Y	G	A	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47163060	SETD2	NM_014159	D1022E	G	T	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47163481	SETD2	NM_014159	S882C	G	C	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47163512	SETD2	NM_014159	Q872E	G	C	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47163754	SETD2	NM_014159	S791L	G	A	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47164283	SETD2	NM_014159	P615T	G	T	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47164380	SETD2	NM_014159	I582M	G	C	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47165126	SETD2	NM_014159	Q334E	G	C	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47165321	SETD2	NM_014159	Q269E	G	C	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL020469_D1	DIAGNOSIS	chr3:47165416	SETD2	NM_014159	S237F	G	A	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL021299_D1	DIAGNOSIS	chr3:47163224	SETD2	NM_014159	S968fs	----	GCTT	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	FRAMESHIFT
SJBALL021324_D1	DIAGNOSIS	chr3:47165069	SETD2	NM_014159	F351_K353>*	TTTTAA	------	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	PROTEINDEL
SJBALL021372_D1	DIAGNOSIS	chr3:47061276	SETD2	NM_014159	K2469*	T	A	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	NONSENSE
SJBALL021372_D1	DIAGNOSIS	chr3:47155365	SETD2	NM_014159	P1571_E5splice	C	A	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	SPLICE
SJBALL021372_D1	DIAGNOSIS	chr3:47059126	SETD2	NM_014159	K2511_E20splice_region	--	CC	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	SPLICE_REGION
SJBALL021514_D1	DIAGNOSIS	chr3:47059133	SETD2	NM_014159	R2510G	G	C	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJBALL021514_D1	DIAGNOSIS	chr3:47165521	SETD2	NM_014159	L202fs	AG	--	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	FRAMESHIFT
SJERG005_D	DIAGNOSIS	chr3:47165670	SETD2	NM_014159	T152fs	-	A	No	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	FRAMESHIFT
SJERG018_D	DIAGNOSIS	chr3:47162984	SETD2	NM_014159	E1048Q	C	G	Not available	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	MISSENSE
SJERG020051_D1	DIAGNOSIS	chr3:47103774	SETD2	NM_014159	N2058fs	--	AT	No	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	FRAMESHIFT
SJERG020300_D1	DIAGNOSIS	chr3:47155487	SETD2	NM_014159	R1532fs	--	CC	No	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	FRAMESHIFT
SJERG020306_D1	DIAGNOSIS	chr3:47059135	SETD2	NM_014159	K2506_A2509fs	GCCAGATGTTT	-----------	No	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	FRAMESHIFT
SJERG020306_D1	DIAGNOSIS	chr3:47147612	SETD2	NM_014159	S1572_E6splice	-----	GGGGT	No	27776115	B-cell Acute Lymphoblastic Leukemia	DUX4/ERG	SPLICE

COSMIC Haematopoietic and Lymphoid Malignancies Cohort

Sample		Genome pos.	Gene	isoform	Mutation	Ref	Alt	Pubmed ID	diagnosis	Class
PARGHW		chr3:47125721	SETD2	NM_014159	R1850fs	-	CC	25790293	acute_lymphoblastic_B_cell_leukaemia	FRAMESHIFT
4-1044673-T1		chr3:47158132	SETD2	NM_014159	R1523C	G	A	25105841	acute_lymphoblastic_B_cell_leukaemia	MISSENSE
PARFTR		chr3:47147534	SETD2	NM_014159	R1598*	G	A	25790293	acute_lymphoblastic_B_cell_leukaemia	NONSENSE
SJBALL021373_D1		chr3:47139530	SETD2	NM_014159	R1686P	C	G	25207766	acute_lymphoblastic_B_cell_leukaemia	MISSENSE
TL04		chr3:47164536	SETD2	NM_014159	C530fs	-	C	26206799	acute_lymphoblastic_T_cell_leukaemia	FRAMESHIFT
TL17		chr3:47163586	SETD2	NM_014159	F847fs	-	G	26206799	acute_lymphoblastic_T_cell_leukaemia	FRAMESHIFT
6831		chr3:47162236	SETD2	NM_014159	R1297fs	-	T	26206799	acute_lymphoblastic_T_cell_leukaemia	FRAMESHIFT
TL43		chr3:47164342	SETD2	NM_014159	S595fs	-	T	26206799	acute_lymphoblastic_T_cell_leukaemia	FRAMESHIFT
TLE34		chr3:47144862	SETD2	NM_014159	C1631S	A	T	23263491	acute_lymphoblastic_T_cell_leukaemia	MISSENSE
TL87		chr3:47165536	SETD2	NM_014159	A197fs	G	AG	26206799	acute_lymphoblastic_T_cell_leukaemia	FRAMESHIFT
SJTALL190		chr3:47162558	SETD2	NM_014159	V1190M	C	T	22237106	acute_lymphoblastic_T_cell_leukaemia	MISSENSE
SJTALL173		chr3:47155452	SETD2	NM_014159	P1534_R1543fs	CCGTCTATTGGAACAATAATCCCCATTT	-	22237106	acute_lymphoblastic_T_cell_leukaemia	FRAMESHIFT
SJTALL199		chr3:47164805	SETD2	NM_014159	R441*	G	A	22237106	acute_lymphoblastic_T_cell_leukaemia	NONSENSE
CN-AML-CR-64-Dx		chr3:47144879	SETD2	NM_014159	R1625H	C	T		acute_myeloid_leukaemia	MISSENSE
SNUH_G16_S1		chr3:47162886	SETD2	NM_014159	M1080I	C	A		acute_myeloid_leukaemia	MISSENSE
CN-AML-CR-64-Dx		chr3:47125269	SETD2	NM_014159	K2001*	T	A		acute_myeloid_leukaemia	NONSENSE
TARGET-20-PARBIU-04A-01D		chr3:47161717	SETD2	NM_014159	P1470L	G	A		acute_myeloid_leukaemia	MISSENSE
TARGET-20-PATDNN-04A-01D		chr3:47125573	SETD2	NM_014159	E1899fs	-	G		acute_myeloid_leukaemia	FRAMESHIFT
TARGET-20-PATDNN-09A-01D		chr3:47125573	SETD2	NM_014159	E1899fs	-	G		acute_myeloid_leukaemia	FRAMESHIFT
TARGET-20-PARASV-04A-02D		chr3:47125223	SETD2	NM_014159	W2016*	C	T		acute_myeloid_leukaemia	NONSENSE
CN-AML-NR-18-Dx		chr3:47165275	SETD2	NM_014159	S284Y	G	T		acute_myeloid_leukaemia	MISSENSE
CN-AML-18-T		chr3:47165275	SETD2	NM_014159	S284Y	G	T		acute_myeloid_leukaemia	MISSENSE
ATL410		chr3:47165283	SETD2	NM_014159	K281fs	T	-	26437031	adult_T_cell_lymphoma-leukaemia	FRAMESHIFT
ATL014		chr3:47165765	SETD2	NM_014159	G121S	C	T	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL382		chr3:47125755	SETD2	NM_014159	E1839*	C	A	26437031	adult_T_cell_lymphoma-leukaemia	NONSENSE
ATL309		chr3:47161709	SETD2	NM_014159	F1473L	A	G	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL074		chr3:47059193	SETD2	NM_014159	R2490W	G	A	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL246		chr3:47161709	SETD2	NM_014159	F1473L	A	G	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL376		chr3:47164157	SETD2	NM_014159	K657*	T	A	26437031	adult_T_cell_lymphoma-leukaemia	NONSENSE
ATL050		chr3:47165560	SETD2	NM_014159	S189F	G	A	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL376		chr3:47163860	SETD2	NM_014159	H756N	G	T	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL376		chr3:47164154	SETD2	NM_014159	V658L	C	A	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL093		chr3:47129662	SETD2	NM_014159	R1740W	G	A	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL320		chr3:47098435	SETD2	NM_014159	V2280fs	-	A	26437031	adult_T_cell_lymphoma-leukaemia	FRAMESHIFT
ATLL_A-01		chr3:47165765	SETD2	NM_014159	G121S	C	T	26574607	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL067		chr3:47162434	SETD2	NM_014159	G1231E	C	T	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
ATL088		chr3:47164103	SETD2	NM_014159	G675R	C	G	26437031	adult_T_cell_lymphoma-leukaemia	MISSENSE
56		chr3:47164880	SETD2	NM_014159	N416Y	T	A	24345752	angioimmunoblastic_T_cell_lymphoma	MISSENSE
23		chr3:47165845	SETD2	NM_014159	N94S	T	C	24345752	angioimmunoblastic_T_cell_lymphoma	MISSENSE
015-08-01TD		chr3:47163901	SETD2	NM_014159	S742*	G	C		chronic_lymphocytic_leukaemia-small_lymphocytic_lymphoma	NONSENSE
141-02-3TD		chr3:47088090	SETD2	NM_014159	Q2329*	G	A		chronic_lymphocytic_leukaemia-small_lymphocytic_lymphoma	NONSENSE
141-02-3TD		chr3:47087975	SETD2	NM_014159	P2366_E16splice	A	C		chronic_lymphocytic_leukaemia-small_lymphocytic_lymphoma	SPLICE
S21_post		chr3:47162208	SETD2	NM_014159	W1306*	C	T	26675346	chronic_lymphocytic_leukaemia-small_lymphocytic_lymphoma	NONSENSE
177-01-9TD		chr3:47162250	SETD2	NM_014159	Q1292fs	C	-		chronic_lymphocytic_leukaemia-small_lymphocytic_lymphoma	FRAMESHIFT
DLBCL1052		chr3:47147599	SETD2	NM_014159	V1576G	A	C	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
DLBCL759		chr3:47163847	SETD2	NM_014159	L760P	A	G	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
U2932		chr3:47163470	SETD2	NM_014159	L886V	G	C	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
DLBCL806		chr3:47163843	SETD2	NM_014159	M761I	C	T	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
DLBCL890		chr3:47142966	SETD2	NM_014159	Y1666C	T	C	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
Ly1		chr3:47098389	SETD2	NM_014159	I2295M	T	C	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
TMD8		chr3:47079245	SETD2	NM_014159	T2421A	T	C	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
Ly10		chr3:47163470	SETD2	NM_014159	L886V	G	C	23292937	diffuse_large_B_cell_lymphoma	MISSENSE
BL26		chr3:47059161	SETD2	NM_014159	T2500del	GGT	-	24241536	hairy_cell_leukaemia	PROTEINDEL
LOXIMVI		chr3:47144880	SETD2	NM_014159	R1625C	G	A	23856246	hairy_cell_leukaemia	MISSENSE

Supplementary Table 2: small guide sequences and primers used

All genomic coordinators are for GRCh37/hg19 (human) or mm10 (mouse)

sgRNA name	**Sequence (without PAM)**	**Reverse complement (without PAM)**	**Genomic Coordinate**
Human *SETD2* exon 3 sgRNA	AATAGGTTTCTCACTGCACT	AGTGCAGTGAGAAACCTATT	chr3:47165851 - 47165870
Mouse *Setd2* exon 3 sgRNA	TCAAGTCGATTTTTGCCCAA	TTGGGCAAAAATCGACTTGA	chr9:110547272 - 110547294
Human *MSH6* sgRNA	CTTGGGGAAGAAGCTGTACA	TGTACAGCTTCTTCCCCAAG	chr2:48010392 - 48010411

Sequencing primer	**Primer Sequence**	**Genomic Coordinate**
Human *SETD2* ex3 forward	GTGGCCTGGATGTTACATGA	chr3:47165660 - 47165679
Human *SETD2* ex3 reverse	GAAGAACAGGGACGACAGAAG	chr3:47165910 - 47165930
Mouse *Setd2* ex3 forward	AACAGGTTTCATCAAAGGACCA	chr9:110547232 - 110547253
Mouse *Setd2* ex3 reverse	GGGAGTTTGGAGAATCACTTTG	chr9:110547410 - 110547431
Human *MSH6* ex1 forward	CGGTAGATGCGGTGCTTT	chr2:48010309 - 48010326
Human *MSH6* ex1 reverse	GAGGTTCTTCGCCTTGGG	chr2:48010571 - 48010588

Supplementary Table 3: Novel clonal mutations identified in 6-thioguanine treated MOLM-13 subclones

Variants present in the respective pre-treatment subclone were subtracted the variants from each post treatment subclone

MOLM-13 Isogenic control no treatment subclone No new mutations identified from pretreatment subclone

MOLM-13 Isogenic control 6-TG treated subclone 1

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	156348109	C	T	RHBG	c.C592T	p.R198W	39.7%	73
2	183291310	G	T	PDE1A	c.C48A	p.I16I	47.5%	61
3	14536386	G	C	GRIP2	c.C3228G	p.R1076G	55.6%	36
4	126238764	G	A	FAT4	c.G1198A	p.G400R	42.7%	75
5	132149747	C	T	SOWAHA	c.C434T	p.P145L	54.6%	33
7	146825798	G	A	CNTNAP2	c.G953A	p.G318D	57.5%	40
10	116049050	G	A	VWA2	c.G1924A	p.G642R	36.8%	114
13	67801322	G	A	PCDH9	c.C1251T	p.N417N	35.1%	97
14	23858825	C	T	MYH6	c.G3836A	p.R1279Q	36.4%	66
14	33290632	G	A	AKAP6	c.G3613A	p.G1205S	53.3%	75
16	72984471	A	C	ZFHX3	c.T371G	p.V124G	43.6%	55
16	72984473	G	T	ZFHX3	c.C369A	p.P123P	44.1%	59
20	48129748	G	A	PTGIS	c.C1075T	p.R359C	38.9%	36
21	43248687	C	T	PRDM15	c.G2467A	p.D823N	58.3%	60

MOLM-13 Isogenic control 6-TG treated subclone 2

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	78267110	G	A	FAM73A	c.G290A	p.R97H	45.5%	22
1	160523933	C	T	CD84	c.G392A	p.R131Q	35.7%	56
2	27445074	G	A	CAD	c.G365A	p.R122Q	46.3%	54
2	165947098	G	T	SCN3A	c.C5565A	p.A1855A	46.0%	74
3	42577714	C	T	VIPR1	c.C1171T	p.R391C	48.8%	43
3	140123527	G	A	CLSTN2	c.G556A	p.E186K	39.7%	58
5	140262837	T	C	PCDHA13	c.T984C	p.I328I	41.2%	97
5	140263396	G	A	PCDHA13	c.G1543A	p.G515S	53.1%	32
6	82459582	G	A	FAM46A	c.C1159T	p.R387W	31.9%	182
6	82459600	T	A	FAM46A	c.A1141T	p.I381F	31.6%	187
6	93964506	T	G	EPHA7	c.A2391C	p.K797N	37.9%	103
6	138550972	G	A	KIAA1244	c.G403A	p.V135M	38.9%	108
7	82583766	T	C	PCLO	c.A6503G	p.E2168G	48.1%	104
7	122763200	C	A	SLC13A1	c.G1330T	p.A444S	50.8%	67
8	90993682	C	G	NBN	c.G241C	p.E81Q	35.0%	40
9	134357188	C	A	PRRC2B	c.C4976A	p.S1659Y	54.6%	44
11	70202345	G	A	PPFIA1	c.G2567A	p.R856H	46.4%	56
13	74289519	C	T	KLF12	c.G1013A	p.R338Q	32.1%	55
13	110435630	A	C	IRS2	c.T2771G	p.F924C	38.5%	78
14	90769118	C	A	NRDE2	c.G1357T	p.D453Y	55.9%	59
14	105397094	G	A	PLD4	c.G733A	p.A245T	52.9%	68
15	99672279	C	A	SYNM	c.C3716A	p.G1238A	30.5%	141
16	56866295	A	G	NUP93	c.A971G	p.D324G	61.5%	52
16	72845599	C	T	ZFHX3	c.G999A	p.S333S	47.4%	38
16	89764248	G	-	SPATA2L	c.769delC	p.L257fs	40.4%	99
17	6676430	A	G	XAF1	c.850-2A>G		45.8%	24

17	27935921	C	T	ANKRD13B	c.C474T	p.S158S	46.9%	128
17	60769650	G	A	MRC2	c.G4278A	p.L1426L	43.5%	46
17	76491149	T	C	DNAH17	c.A5934G	p.E1978E	45.8%	48
19	17008740	C	T	CPAMD8	c.G5055A	p.T1685T	38.4%	125
19	33642127	C	T	WDR88	c.C720T	p.P240P	31.3%	64
23	57935902	T	C	ZXDA	c.A953G	p.K318R	100.0%	29

MOLM-13 Isogenic control 6-TG treated subclone 3

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	156347917	C	T	RHBG	c.C511T	p.L171F	39.4%	66
3	151011994	G	A	GPR87	c.C1040T	p.S347L	50.0%	46
4	8583363	C	T	GPR78	c.C654T	p.A218A	42.3%	52
5	145439604	G	A	SH3RF2	c.G1731A	p.T577T	52.9%	70
6	110301098	G	A	GPR6	c.G783A	p.L261L	34.2%	79
8	1871138	T	C	ARHGEF10	c.T2152C	p.Y718H	38.1%	21
9	127215404	T	C	GPR144	c.T428C	p.L143P	45.5%	22
9	131296165	G	T	GLE1	c.G1581T	p.K527N	50.0%	44
11	4621850	G	A	TRIM68	c.C1114T	p.L372L	47.0%	66
11	6422898	C	T	APBB1	c.G632A	p.R211H	43.5%	138
11	62455503	C	T	LRRN4CL	c.G478A	p.G160R	53.3%	92
13	43934166	C	A	ENOX1	c.G410T	p.R137L	30.4%	79
13	97999300	C	A	MBNL2	c.C783A	p.A261A	48.4%	31
16	3142715	G	A	ZSCAN10	c.C59T	p.P20L	47.2%	53
16	30667382	G	A	PRR14	c.G1508A	p.R503Q	51.4%	111
19	7619455	G	C	PNPLA6	c.G2480C	p.R827P	35.9%	64
19	39963862	G	A	SUPT5H	c.G2278A	p.G760S	32.6%	141
19	51298137	C	G	ACPT	c.C1081G	p.R361G	51.0%	49
20	10604012	C	T	SLX4IP	c.C1212T	p.Y404Y	53.9%	39
22	42294681	G	A	SREBF2	c.G2634A	p.T878T	39.4%	33
23	153674034	G	A	FAM50A	c.G165A	p.A55A	100.0%	22

MOLM-13 Isogenic control 6-TG treated subclone 4

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	1277511	C	T	DVL1	c.G388A	p.G130R	50.0%	54
1	27697450	C	A	FCN3	c.G407T	p.R136L	52.0%	25
1	40702413	G	T	RLF	c.G2039T	p.R680L	39.3%	83
1	75038380	C	G	C1orf173	c.G3014C	p.R1005P	48.7%	117
4	42400255	C	T	SHISA3	c.C182T	p.A61V	53.9%	39
4	183721223	G	A	TENM3	c.G7819A	p.V2607M	42.0%	69
8	125061938	C	T	FER1L6	c.C2815T	p.P939S	41.9%	31
10	64028317	G	A	RTKN2	c.C53T	p.T18I	31.0%	71
10	126715250	C	T	CTBP2	c.G1079A	p.R360Q	39.7%	58
11	73130956	G	A	FAM168A	c.C240T	p.T80T	50.0%	12
12	120784115	G	C	MSI1	c.C870G	p.P290P	39.6%	48
14	103410510	C	T	CDC42BPB	c.G4126A	p.V1376M	48.6%	72
15	73615848	C	A	HCN4	c.G2586T	p.L862L	41.7%	36
15	83335614	C	T	AP3B2	c.G1737A	p.A579A	48.5%	33
16	310005	G	A	ITFG3	c.G423A	p.S141S	42.4%	33
16	734820	C	T	WDR24	c.G2287A	p.G763S	52.5%	40
17	79860510	G	C	NPB	c.G264C	p.Q88H	50.0%	38

19	15734844	A	T	CYP4F8	c.A1055T	p.E351V	30.2%	43
19	48953937	G	A	GRWD1	c.G697A	p.G233S	53.9%	52
21	32493037	G	C	TIAM1	c.C4425G	p.P1475P	55.9%	93
22	31979878	G	A	SFI1	c.G1020A	p.W340X	36.4%	22
22	31979889	G	A	SFI1	c.G1031A	p.R344Q	42.9%	21
22	46725991	C	G	GTSE1	c.C2184G	p.D728E	62.2%	45

MOLM-13 Isogenic control 6-TG treated subclone 5

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	156348109	C	T	RHBG	c.C592T	p.R198W	36.9%	84
2	183291310	G	T	PDE1A	c.C48A	p.I16I	45.8%	48
3	14536386	G	C	GRIP2	c.C3228G	p.R1076G	56.1%	41
4	126238764	G	A	FAT4	c.G1198A	p.G400R	49.5%	93
5	132149747	C	T	SOWAHA	c.C434T	p.P145L	46.9%	32
7	146825798	G	A	CNTNAP2	c.G953A	p.G318D	53.6%	56
10	116049050	G	A	VWA2	c.G1924A	p.G642R	32.0%	122
13	67801322	G	A	PCDH9	c.C1251T	p.N417N	30.1%	113
14	23858825	C	T	MYH6	c.G3836A	p.R1279Q	34.7%	75
14	33290632	G	A	AKAP6	c.G3613A	p.G1205S	55.6%	72
16	72984471	A	C	ZFHX3	c.T371G	p.V124G	37.9%	58
16	72984473	G	T	ZFHX3	c.C369A	p.P123P	40.0%	60
20	48129748	G	A	PTGIS	c.C1075T	p.R359C	52.6%	19
21	43248687	C	T	PRDM15	c.G2467A	p.D823N	58.5%	53

MOLM-13 Isogenic control 6-TG treated subclone 6

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	1887180	C	T	KIAA1751	c.G2126A	p.R709Q	48.1%	52
1	10336391	G	A	KIF1B	c.G953A	p.R318Q	30.3%	76
1	16053810	G	A	PLEKHM2	c.G1243A	p.D415N	43.3%	67
1	89734520	C	A	GBP5	c.G210T	p.T70T	55.1%	49
1	231339670	C	T	TRIM67	c.C1592T	p.T531M	37.0%	54
1	237791239	G	A	RYR2	c.G6299A	p.R2100Q	34.3%	105
3	49314156	G	A	C3orf62	c.C150T	p.S50S	40.6%	69
4	126412621	G	T	FAT4	c.G14644T	p.D4882Y	48.1%	79
4	144135928	G	C	USP38	c.G2799C	p.T933T	45.3%	64
5	115782861	G	A	SEMA6A	c.C2541T	p.A847A	60.0%	104
6	30593405	A	C	MRPS18B	c.A608C	p.Y203S	31.8%	66
6	30879211	C	A	GTF2H4	c.C676A	p.R226R	38.5%	64
6	30879212	G	A	GTF2H4	c.G677A	p.R226Q	39.7%	63
6	46684751	G	A	PLA2G7	c.C192T	p.S64S	32.7%	107
9	100854208	C	A	TRIM14	c.G776T	p.R259L	45.8%	24
11	11454221	G	A	GALNTL4	c.C542T	p.T181M	53.1%	64
11	102395704	G	A	MMP7	c.C576T	p.F192F	50.0%	24
15	40544553	C	T	C15orf56	c.G419A	p.R140Q	54.3%	35
17	31091908	G	A	MYO1D	c.C1023T	p.D341D	40.9%	22
19	10224556	C	G	P2RY11	c.C267G	p.L89L	38.3%	128
20	61299525	G	A	SLCO4A1	c.G1800A	p.T600T	54.1%	74
21	42749766	C	A	MX2	c.C300A	p.C100X	57.8%	44

MOLM-13 SETD2 clone 1 no treatment subclone

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
7	92123640	T	C	PEX1	c.A2997G	p.L999L	37.5%	32
16	20803378	G	A	ACSM3	c.G1381A	p.D461N	51.9%	104
19	7267663	G	A	INSR	c.C345T	p.F115F	35.1%	111
19	18332952	C	T	PDE4C	c.G424A	p.A142T	41.0%	39

MOLM-13 SETD2 clone 1 6-TG treated subclone 1

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	9416635	G	C	SPSB1	c.G685C	p.G229R	42.4%	59
1	112269921	C	T	FAM212B	c.G563A	p.R188H	44.5%	137
1	151065741	G	A	GABPB2	c.G350A	p.R117Q	33.9%	62
1	155429656	C	T	ASH1L	c.G5018A	p.R1673Q	33.9%	59
1	226574110	C	T	PARP1	c.G751A	p.E251K	29.4%	34
1	228475649	C	T	OBSCN	c.C11086T	p.L3696F	35.8%	165
2	144903256	C	T	GTDC1	c.G230A	p.R77Q	57.9%	57
2	220348881	C	A	SPEG	c.C6696A	p.P2232P	58.1%	86
3	52840153	T	C	ITIH3	c.T1943C	p.Y647Y	52.9%	51
4	83838545	G	A	THAP9	c.G1180A	p.D394N	58.1%	129
4	154243913	C	T	TRIM2	c.C1896T	p.N632N	46.7%	30
4	155412111	G	A	DCHS2	c.C397T	p.R133C	44.2%	52
4	186573876	C	T	SORBS2	c.G31A	p.D11N	57.1%	56
5	169230141	G	A	DOCK2	c.G2634A	p.Q878Q	53.6%	28
6	13597247	C	G	SIRT5	c.C294G	p.R98G	25.9%	108
6	26252176	C	T	HIST1H2BH	c.C298T	p.R100C	34.2%	82
6	30037001	G	A	PPP1R11	c.G299A	p.R100H	33.3%	48
6	34100794	C	T	GRM4	c.G480A	p.S160S	25.0%	148
6	99848490	G	A	PNISR	c.C2344T	p.R782X	30.1%	156
6	147047289	T	C	ADGB	c.T2308C	p.F770L	30.3%	122
7	45120355	C	T	NACAD	c.G4558A	p.E1520K	50.8%	67
8	145012372	G	A	PLEC	c.C115T	p.R39C	27.0%	63
9	34996776	C	T	DNAJB5	c.C942T	p.I314I	52.6%	78
9	35740951	G	A	GBA2	c.C897T	p.D299D	51.6%	97
9	93606245	G	A	SYK	c.G65A	p.R22Q	47.9%	48
9	96054847	G	A	WNK2	c.G5100A	p.S1700S	63.0%	81
10	88415952	C	T	OPN4	c.C185T	p.T62M	35.6%	73
10	133787409	C	T	BNIP3	c.G85A	p.G29R	29.7%	37
12	52713145	G	A	KRT83	c.C388T	p.R130C	51.7%	29
12	113629398	C	T	C12orf52	c.C586T	p.R196W	34.4%	150
12	133294343	G	A	PGAM5	c.G544A	p.E182K	43.2%	43
13	28498641	G	T	PDX1	c.G655T	p.G219W	25.0%	16
13	28542991	C	T	CDX2	c.G153A	p.A51A	37.9%	87
14	50734598	C	T	L2HGDH	c.G937A	p.V313I	47.1%	70
14	102973937	C	T	ANKRD9	c.G290A	p.R97Q	47.1%	17
15	65621374	G	A	IGDCC3	c.C2318T	p.T773M	46.5%	43
15	66015267	C	T	DENND4A	c.G1507A	p.V503I	35.1%	37
15	101569375	G	A	LRRK1	c.G2901A	p.T967T	44.8%	67
16	15122739	G	A	PDXDC1	c.G1209A	p.P403P	44.4%	18
16	25238440	G	A	AQP8	c.G654A	p.A218A	45.5%	77
16	71571025	C	T	CHST4	c.C445T	p.R149W	45.5%	132
16	75148128	C	T	LDHD	c.G634A	p.G212S	47.3%	55

16	84353089	G	A	WFDC1	c.G474A	p.S158S	65.0%	40
17	10543394	C	T	MYH3	c.G2601A	p.S867S	55.4%	74
17	35299591	G	A	LHX1	c.G770A	p.R257Q	58.3%	24
17	37762108	C	T	NEUROD2	c.G745A	p.A249T	59.6%	52
19	1986631	G	A	BTBD2	c.C1434T	p.Y478Y	36.7%	60
19	3526383	C	T	FZR1	c.C388T	p.T129M	31.0%	42
19	3833724	G	A	ZFR2	c.C317T	p.P106L	31.5%	73
19	12902612	C	A	JUNB	c.C27A	p.F9L	34.4%	151
19	18054501	G	A	CCDC124	c.G649A	p.V217M	44.0%	91
19	44351826	G	A	ZNF283	c.G1073A	p.R358H	53.9%	78
20	55026995	G	A	CASS4	c.G601A	p.V201I	46.3%	67
21	38480702	G	A	TTC3	c.G856A	p.G286S	55.0%	20
21	42551516	G	T	PLAC4	c.C40A	p.L14I	44.4%	9
23	15373324	G	A	FIGF	c.C589T	p.R197C	100.0%	36
23	152845617	C	T	ATP2B3	c.C3524T	p.P1175L	100.0%	54

MOLM-13 SETD2 clone 1 6-TG treated subclone 2

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	9165579	G	A	GPR157	c.C758T	p.P253L	58.8%	51
2	179368547	A	G	PLEKHA3	c.A836G	p.E279G	45.5%	77
3	186300546	C	T	DNAJB11	c.C724T	p.R242X	39.0%	41
4	57325538	G	A	PAICS	c.G1114A	p.G371D	36.5%	52
4	130003466	C	A	SCLT1	c.G97T	p.V33L	58.1%	31
4	184240817	A	G	CLDN22	c.T555C	p.C185C	36.2%	58
4	184240822	G	T	CLDN22	c.C550A	p.H184N	32.1%	56
5	79854550	C	T	ANKRD34B	c.G1289A	p.R430Q	57.3%	82
8	29996212	G	A	MBOAT4	c.C180T	p.A60A	30.6%	36
8	144732816	G	A	ZNF623	c.G654A	p.T218T	37.3%	158
8	145113797	G	A	OPLAH	c.C466T	p.R156C	32.5%	114
10	77158714	C	A	ZNF503	c.G1734T	p.S578S	33.1%	133
10	114044382	G	A	TECTB	c.G166A	p.G56R	35.6%	90
14	105167919	G	T	INF2	c.G217T	p.G73C	35.9%	53
17	40688647	G	A	NAGLU	c.G357A	p.G119G	67.7%	31
18	46343709	C	T	CTIF	c.C1495T	p.R499C	32.8%	67
19	12786940	T	G	DHPS	c.A905C	p.Y302S	39.8%	88
19	55341682	G	A	KIR3DL1	c.G1287A	p.T429T	53.3%	137
19	55450893	G	A	NLRP7	c.C1294T	p.R432X	59.6%	52
20	44472914	G	A	ACOT8	c.C634T	p.R212W	40.3%	62
21	47842033	G	A	PCNT	c.G7174A	p.V2392M	50.0%	54

MOLM-13 SETD2 clone 1 6-TG treated subclone 3

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	33318687	G	A	S100PBP	c.G1032A	p.S344S	62.1%	29
1	215848914	C	T	USH2A	c.G12339A	p.L4113L	35.7%	98
1	225605797	A	C	LBR	c.T726G	p.N242K	31.8%	66
1	228482059	G	A	OBSCN	c.G12625A	p.G4209R	30.9%	222
2	179664242	C	T	TTN	c.G886A	p.V296M	45.7%	35
4	80828600	G	A	ANTXR2	c.C1450T	p.R484X	47.0%	66
6	8097577	C	A	EEF1E1	c.G211T	p.V71F	32.0%	194
7	45632413	G	C	ADCY1	c.G695C	p.R232P	43.3%	134

7	129856219	G	A	C7orf45	c.G644A	p.R215Q	55.4%	74
8	1497006	C	-	DLGAP2	c.147delC	p.P49fs	43.8%	73
8	97614665	G	T	SDC2	c.G215T	p.R72L	33.3%	84
9	27949928	C	T	LINGO2	c.G742A	p.G248S	50.0%	80
9	96002095	G	T	WNK2	c.G1379T	p.R460M	53.7%	41
11	18566292	C	T	UEVLD	c.G824A	p.R275Q	54.8%	42
11	124750467	G	A	ROBO3	c.G4112A	p.R1371Q	43.6%	39
13	103386377	G	A	CCDC168	c.C16670T	p.P5557L	36.3%	190
13	110437001	G	A	IRS2	c.C1400T	p.P467L	31.6%	19
13	114265317	C	G	TFDP1	c.C19G	p.L7V	34.6%	52
15	41247882	G	A	CHAC1	c.G570A	p.A190A	56.3%	80
16	837081	C	T	RPUSD1	c.G405A	p.S135S	57.1%	77
19	39056105	C	G	RYR1	c.C13131G	p.T4377T	45.5%	22

MOLM-13 SETD2 clone 1 6-TG treated subclone 4

Chrom	Position	Ref	Var	Gene	cDNA	aa	Allele Fraction	Fold Coverage
1	9416635	G	C	SPSB1	c.G685C	p.G229R	58.2%	67
1	109792706	G	A	CELSR2	c.G5A	p.R2Q	52.8%	36
1	112269921	C	T	FAM212B	c.G563A	p.R188H	50.0%	144
1	151065741	G	A	GABPB2	c.G350A	p.R117Q	27.6%	58
1	155429656	C	T	ASH1L	c.G5018A	p.R1673Q	37.8%	74
1	226574110	C	T	PARP1	c.G751A	p.E251K	30.2%	63
1	228475649	C	T	OBSCN	c.C11086T	p.L3696F	38.9%	185
2	144903256	C	T	GTDC1	c.G230A	p.R77Q	62.5%	64
2	220348881	C	A	SPEG	c.C6696A	p.P2232P	52.8%	127
3	52840153	T	C	ITIH3	c.T1943C	p.Y647Y	44.6%	56
4	83838545	G	A	THAP9	c.G1180A	p.D394N	45.5%	132
4	154243913	C	T	TRIM2	c.C1896T	p.N632N	53.2%	47
4	155412111	G	A	DCHS2	c.C397T	p.R133C	44.8%	58
4	186573876	C	T	SORBS2	c.G31A	p.D11N	33.9%	59
5	169230141	G	A	DOCK2	c.G2634A	p.Q878Q	38.5%	26
6	13597247	C	G	SIRT5	c.C294G	p.R98G	37.3%	102
6	26252176	C	T	HIST1H2BH	c.C298T	p.R100C	34.5%	113
6	30037001	G	A	PPP1R11	c.G299A	p.R100H	25.3%	91
6	34100794	C	T	GRM4	c.G480A	p.S160S	35.2%	165
6	99848490	G	A	PNISR	c.C2344T	p.R782X	35.2%	182
6	147047289	T	C	ADGB	c.T2308C	p.F770L	38.8%	134
7	45120355	C	T	NACAD	c.G4558A	p.E1520K	56.8%	88
8	145012372	G	A	PLEC	c.C115T	p.R39C	34.7%	72
9	34996776	C	T	DNAJB5	c.C942T	p.I314I	49.4%	85
9	35740951	G	A	GBA2	c.C897T	p.D299D	48.9%	137
9	93606245	G	A	SYK	c.G65A	p.R22Q	47.6%	63
9	96054847	G	A	WNK2	c.G5100A	p.S1700S	46.5%	101
10	88415952	C	T	OPN4	c.C185T	p.T62M	38.1%	84
10	133787409	C	T	BNIP3	c.G85A	p.G29R	47.4%	38
12	52713145	G	A	KRT83	c.C388T	p.R130C	53.1%	32
12	113629398	C	T	C12orf52	c.C586T	p.R196W	34.7%	193
12	133294343	G	A	PGAM5	c.G544A	p.E182K	28.4%	87
13	28498641	G	T	PDX1	c.G655T	p.G219W	39.5%	43
13	28542991	C	T	CDX2	c.G153A	p.A51A	27.5%	91

14	50734598	C	T	L2HGDH	c.G937A	p.V313I	49.4%	77
14	102973937	C	T	ANKRD9	c.G290A	p.R97Q	50.0%	28
15	65621374	G	A	IGDCC3	c.C2318T	p.T773M	50.0%	48
15	66015267	C	T	DENND4A	c.G1507A	p.V503I	47.4%	19
15	101569375	G	A	LRRK1	c.G2901A	p.T967T	37.1%	97
16	15122739	G	A	PDXDC1	c.G1209A	p.P403P	38.9%	18
16	25238440	G	A	AQP8	c.G654A	p.A218A	48.5%	66
16	71571025	C	T	CHST4	c.C445T	p.R149W	49.8%	197
16	75148128	C	T	LDHD	c.G634A	p.G212S	38.5%	78
16	84353089	G	A	WFDC1	c.G474A	p.S158S	41.8%	55
17	10543394	C	T	MYH3	c.G2601A	p.S867S	50.0%	84
17	35299591	G	A	LHX1	c.G770A	p.R257Q	43.3%	30
17	37762108	C	T	NEUROD2	c.G745A	p.A249T	57.0%	100
19	1986631	G	A	BTBD2	c.C1434T	p.Y478Y	44.9%	78
19	3526383	C	T	FZR1	c.C388T	p.T129M	33.3%	72
19	3833724	G	A	ZFR2	c.C317T	p.P106L	33.7%	95
19	12902612	C	A	JUNB	c.C27A	p.F9L	25.5%	157
19	18054501	G	A	CCDC124	c.G649A	p.V217M	33.3%	117
19	44351826	G	A	ZNF283	c.G1073A	p.R358H	54.6%	77
20	55026995	G	A	CASS4	c.G601A	p.V201I	50.7%	73
21	38480702	G	A	TTC3	c.G856A	p.G286S	47.1%	17
21	42551516	G	T	PLAC4	c.C40A	p.L14I	31.6%	19
23	15373324	G	A	FIGF	c.C589T	p.R197C	100.0%	40
23	152845617	C	T	ATP2B3	c.C3524T	p.P1175L	97.9%	47