

## SUPPLEMENTAL MATERIAL

### Cytogenetic analysis and cohort definitions

Cytogenetic aberrations and composite karyotypes were described according to the International System for Human Cytogenomic Nomenclature 2016 guidelines<sup>1</sup>. Complex karyotype was defined as having 3 or more chromosomal abnormalities in the absence of 1 of the WHO-designated recurring translocations or inversions, that is t(8;21), inv(16) or t(16;16), t(9;11), t(v;11)(v;q23.3), t(6;9), inv(3) or t(3;3) and AML with *BCR-ABL1*<sup>2</sup>. Composite karyotypes with  $\geq$  five cytogenetic aberrations were considered as markers of higher clonal heterogeneity. FISH analyses for *TP53* deletions were performed using the Vysis LSI *TP53/CEP17* probe (#05N56-020, Abbott Molecular).

### *TP53* isoform expression

Isoform expression (GRCh38 v84) was computed using Kallisto v43.0 (PMID 27043002). For each specimen, we either summed up 1/ expression of all isoforms to obtain gene expression values, 2/ isoforms encoding full-length or delta 40 p53 protein isoforms (ENST00000413465.6, ENST00000359597.8, ENST00000455263.6, ENST00000420246.6, ENST00000617185.4, ENST00000269305.8, ENST00000445888.6, ENST00000615910.4, ENST00000622645.4, ENST00000620739.4, ENST00000610538.4, ENST00000619485.4, ENST00000610292.4), 3/ isoforms encoding delta 133 or delta 160 p53 (ENST00000618944.4, ENST00000619186.4, ENST00000504290.5, ENST00000610623.4, ENST00000510385.5, ENST00000504937.5), or 4/ non-coding isoforms (containing retained introns, non-sense-mediated decay products, or with incomplete open reading frames; i.e. ENST00000635293.1, ENST00000576024.1, ENST00000509690.5, ENST00000514944.5, ENST00000574684.1, ENST00000505014.5, ENST00000508793.5, ENST00000604348.5, ENST00000503591.1).

### Normal hematopoietic cells

Control cord blood (CB) cells were collected from consenting mothers at the Charles LeMoyné Hospital (Greenfield Park, QC, Canada). Before chemical screening, CD34<sup>+</sup> CB cells were isolated using the EasySep kit (StemCell Technologies) and cultivated for 6 days in UM171-supplemented media as described previously<sup>3</sup>. CB cells were screened in StemSpan-ACF (StemCell Technologies 09855) containing 100ng/mL SCF, 100ng/mL TPO, 50ng/mL FLT3-L, 1X GlutaMax, 10 $\mu$ g/mL LDL, 500 nM SR1 and 35 nM UM171. Human CD34<sup>+</sup> control mobilized peripheral blood (mpB) from a single healthy donor were isolated by CD34 positive selection using Clinimacs<sup>TM</sup> (Miltenyi). These mpB CD34<sup>+</sup> cells were cultured in the same conditions as the CB CD34<sup>+</sup> cells, with addition of 50 ng/mL Interleukin-6.

### *In vivo* experimentation

All animal procedures complied with recommendations of the Canadian Council on Animal Care and were approved by the Deontology Committee on Animal Experimentation at University of Montreal. NSG mice were purchased from Jackson Laboratory and bred in a pathogen-free animal facility. Eight to twelve-week-old female littermates were randomly assigned to experimental groups and transplanted with leukemic cells *via* the tail vein. Complex karyotype *TP53*-null HL-60 cells<sup>4</sup> and the adverse cytogenetic risk/*TP53* mutated human AML specimen 09H046 (also bears monosomy 17 and mutation in *RUNX1*, *DNMT3A*, *TET2*, *BCOR*, *CEBPA*, *CUX1*, *KMT2C*, *KMT2D*, *NF1*, *SMC5*,

*STAG2* and *USP7* genes) were chosen as relevant models. Six days after transplantation, mice were treated with either volasertib (IV, 2 times a week for 4 weeks at 10mg/kg, formulated in HCl and freshly diluted in 0.9% NaCl), or cytarabine (IP for 5 consecutive days at 50mg/kg, freshly diluted in phosphate buffered saline (PBS)). Vehicle treated mice received both PBS (IP) and 0.9% NaCl (IV). Daily monitoring of mice for symptoms of disease (weight loss, ruffled coat, hunched back and reduced motility) determined the end point for each animal. Leukemia development in sacrificed animals was confirmed by detection of high percentages (>70%) of human CD45 positive cells in the bone marrow and/or spleen by flow cytometry analysis.

### **Flow cytometry analyses**

Bone marrow and spleen were collected and/or dissected and made into single cell suspensions for analysis by flow cytometry (BD Canto II cytometer). Percentage of leukemic cell engraftment was assessed using the following antibodies: anti-human CD45 Pacific Blue (BioLegend #304029) and anti-mouse CD45.1 APC-eFluor780 (eBioscience #47-0453-82). Results were analyzed with FlowJo software.

### **Statistical analyses**

Fisher's exact test was used in the analysis of contingency tables. Analysis of differential gene expression was performed using the Wilcoxon rank-sum test and the false discovery rate (FDR) method was applied for global gene analysis as previously described<sup>11</sup>. Differences in response to small molecules between genetic groups were evaluated using a Wilcoxon rank-sum test performed on IC<sub>50</sub> values in R version 3.1.2. Clustering was performed in python 3.6.2 using the Seaborn library.

1. An International System for Human Cytogenomic Nomenclature (2016) Reprint of: Cytogenetic and Genome Research Vol. 149; 2016.
2. Dohner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood*. 2017;129(4):424-447.
3. Fares I, Chagraoui J, Gareau Y, et al. Cord blood expansion. Pyrimidoindole derivatives are agonists of human hematopoietic stem cell self-renewal. *Science*. 2014;345(6203):1509-1512.
4. Liang JC, Ning Y, Wang RY, et al. Spectral karyotypic study of the HL-60 cell line: detection of complex rearrangements involving chromosomes 5, 7, and 16 and delineation of critical region of deletion on 5q31.1. *Cancer Genet Cytogenet*. 1999;113(2):105-109.

## **SUPPLEMENTAL TABLES**

### **Table S1**

Genes included in the mutational analysis

### **Table S2**

*TP53* mutations in complex karyotype AML

### **Table S3**

Mutations identified in complex karyotype AML

### **Table S4**

Association between complex karyotype AML and mutations

### **Table S5**

Compounds included in the preliminary screen

### **Table S6**

Samples included in the preliminary screen

### **Table S7**

Drug responses in the preliminary screen

### **Table S8**

Samples included in the validation screen

### **Table S9**

Drug responses in the validation screen

### **Table S10**

Gene correlation in AML using MiSTIC

### **Table S11**

Genes included in hallmark G2M checkpoint

### **Table S12**

Gene set enrichment analysis (GSEA) in CK AML

**TABLE S1**

Type	Gene
Mutation	<i>APC</i>
Mutation	<i>ARID1A</i>
Mutation	<i>ASXL1</i>
Mutation	<i>ASXL2</i>
Mutation	<i>ATRX</i>
Mutation	<i>BCOR</i>
Mutation	<i>BCORL1</i>
Mutation	<i>BIRC3</i>
Mutation	<i>BRAF</i>
Mutation	<i>CALR</i>
Fusion gene	<i>CBFB-MYH11</i>
Mutation	<i>CBL</i>
Mutation	<i>CBLB</i>
Mutation	<i>CBLC</i>
Mutation	<i>CDKN2A</i>
Mutation	<i>CEBPA</i>
Mutation	<i>CEBPB</i>
Mutation	<i>CEBPD</i>
Mutation	<i>CEBPE</i>
Mutation	<i>CEBPG</i>
Mutation	<i>CEBPZ</i>
Mutation	<i>CREBBP</i>
Mutation	<i>CSF3R</i>
Mutation	<i>CTNNA1</i>
Mutation	<i>CUX1</i>
Mutation	<i>DDX41</i>
Mutation	<i>DNMT3A</i>
Mutation	<i>EED</i>
Mutation	<i>EP300</i>
Mutation	<i>ETV6</i>
Fusion gene	<i>EVI1</i> (several rearrangements)
Mutation	<i>EZH2</i>
Mutation	<i>FBXW7</i>

Mutation	<i>FLT3</i>
Mutation	<i>GATA1</i>
Mutation	<i>GATA2</i>
Mutation	<i>GNAS</i>
Mutation	<i>H3F3A</i>
Mutation	<i>HIST1H3F</i>
Mutation	<i>HIST1H3H</i>
Mutation	<i>HRAS</i>
Mutation	<i>IDH1</i>
Mutation	<i>IDH2</i>
Mutation	<i>IKZF1</i>
Mutation	<i>IRF1</i>
Mutation	<i>JAK1</i>
Mutation	<i>JAK2</i>
Mutation	<i>JAK3</i>
Mutation	<i>KDM6A</i>
Mutation	<i>KIT</i>
Mutation	<i>KMT2A</i>
Mutation	<i>KMT2B</i>
Mutation	<i>KMT2C</i>
Mutation	<i>KMT2D</i>
Mutation	<i>KRAS</i>
Fusion gene	<i>MLL</i> (several rearrangements)
Fusion gene	<i>ML-RARA</i>
Mutation	<i>MPL</i>
Mutation	<i>MYC</i>
Mutation	<i>MYD88</i>
Mutation	<i>NF1</i>
Mutation	<i>NOTCH1</i>
Mutation	<i>NPM1</i>
Mutation	<i>NRAS</i>
Fusion gene	<i>NUP98-NSD1</i>
Mutation	<i>PHF6</i>
Mutation	<i>PTEN</i>
Mutation	<i>PTPN11</i>

Mutation	<i>RAD21</i>
Mutation	<i>RHOA</i>
Mutation	<i>RUNX1</i>
Fusion gene	<i>RUNX1-RUNX1T1</i>
Mutation	<i>SETBP1</i>
Mutation	<i>SETD2</i>
Mutation	<i>SF3B1</i>
Mutation	<i>SH2B3</i>
Mutation	<i>SMARCA4</i>
Mutation	<i>SMC1A</i>
Mutation	<i>SMC3</i>
Mutation	<i>SMC5</i>
Mutation	<i>SPI1</i>
Mutation	<i>SRSF2</i>
Mutation	<i>STAG1</i>
Mutation	<i>STAG2</i>
Mutation	<i>STAT3</i>
Mutation	<i>STAT5A</i>
Mutation	<i>STAT5B</i>
Mutation	<i>SUZ12</i>
Mutation	<i>TET2</i>
Mutation	<i>TP53</i>
Mutation	<i>U2AF1</i>
Mutation	<i>USP7</i>
Mutation	<i>WHSC1</i>
Mutation	<i>WT1</i>
Mutation	<i>ZBTB7A</i>
Mutation	<i>ZMYM3</i>
Mutation	<i>ZRSR2</i>



11H145	1	G245D	chr17:7577547	0.961	.	.	positive
11H170	0	.	.	.	.	.	negative
11H175	0	.	.	.	.	.	negative
11H177	1	V216G	chr17:7578202	0.9351	.	.	positive
11H187	1	E349-	chr17:7573979	0.7601	Q136*	chr17:7578524	0.1265
12H012	1	C135R	chr17:7578527	0.9718	.	.	negative
12H055	0	.	.	.	.	.	negative
12H058	1	R248W	chr17:7577539	0.9459	.	.	positive
12H067	1	H179Y	chr17:7578395	0.9931	.	.	negative
12H096	0	.	.	.	.	.	negative
12H106	1	Y234C	chr17:7577580	0.9911	.	.	positive
12H117	1	R248Q	chr17:7577538	1	.	.	negative
12H138	0	.	.	.	.	.	negative
12H149	0	.	.	.	.	.	negative
12H170	1	C124-	chr17:7579316	.	.	.	positive
13H018	1	I195T	chr17:7578265	0.8573	.	.	positive
13H056	1	V272M	chr17:7577124	0.3022	.	.	negative
13H141	1	K132-	chr17:7578535	0.98	.	.	positive
13H150	0	.	.	.	.	.	negative



**TABLE S3**

gene	sample	mutation	position	VAF	transcript	method
ASXL1	10H113	G643fsX	chr20:31022441	0.2439	NM_015338	casava
ASXL1	07H038	Q708X	chr20:31022637	0.4547	NM_015338	kmer
BRAF	07H038	R575K	chr7:140454004	0.4828	NM_004333	casava
CALR	12H138	L367 (del52)	chr19:13054572	0.375	NM_004343	kmer
CALR	11H044	L367 (del52)	chr19:13054572	0.334	NM_004343	kmer
CALR	10H130	L367 (del52)	chr19:13054572	0.428	NM_004343	kmer
CBL	12H058	C396R	chr11:119148966	0.6871	NM_005188	casava
CBL	02H026	C416Y	chr11:119149239	0.4242	NM_005188	casava
CEBPA	06H029	A295T	chr19:33792438	0.5082	NM_004364	casava
CREBBP	12H055	Q1765fsX	chr16:3779754	0.3933	NM_004380	casava
CSF3R	11H175	Q741X	chr1:36932248	0.5082	NM_000760	casava
CSF3R	12H106	T618I	chr1:36933434	0.0562	NM_000760	kmer
DNMT3A	09H057	R882H	chr2:25457242	0.1798	NM_175629	kmer
DNMT3A	06H016	R882H	chr2:25457242	0.5071	NM_175629	kmer
DNMT3A	03H090	R882H	chr2:25457242	0.446	NM_175629	kmer
DNMT3A	13H150	I705T	chr2:25463568	0.4897	NM_175629	casava
DNMT3A	10H078	S669fsX	chr2:25464505	0.3182	NM_175629	casava
DNMT3A	12H117	V665M	chr2:25464520	0.5723	NM_175629	casava
DNMT3A	12H170	L508fsX	chr2:25468153	0.2308	NM_175629	casava
DNMT3A	10H014	R379C	chr2:25469633	0.6222	NM_175629	casava
EED	09H085	W364C	chr11:85988147	0.4222	NM_152991	casava
EZH2	13H056	R684C	chr7:148506462	0.768	NM_004456	casava
EZH2	06H029	L589P	chr7:148511136	0.3521	NM_004456	casava
FLT3	04H132	D835H	chr13:28592642	0.0813	NM_004119	kmer
FLT3	06H074	A680V	chr13:28602329	0.5276	NM_004119	casava
FLT3	10H078	E596 (ITD)	chr13:28608268	0.5771	NM_004119	kmer
FLT3	03H090	S585 (ITD)	chr13:28608303	0.6822	NM_004119	kmer
FLT3	07H156	V581 (ITD)	chr13:28608314	0.1105	NM_004119	kmer
IDH1	11H187	R132C	chr2:209113113	0.5554	NM_005896	kmer
IDH2	10H113	R140Q	chr15:90631934	0.5513	NM_002168	kmer
IDH2	13H150	R140Q	chr15:90631934	0.5003	NM_002168	kmer
IDH2	10H014	R140Q	chr15:90631934	0.4817	NM_002168	kmer
JAK2	09H054	V617F	chr9:5073770	0.7162	NM_004972	kmer
JAK2	03H030	V617F	chr9:5073770	0.766	NM_004972	kmer
JAK2	12H058	V617F	chr9:5073770	0.5512	NM_004972	kmer
JAK2	09H085	V617F	chr9:5073770	0.9849	NM_004972	kmer
KMT2A	13H141	PTD	chr11:118339489	NA	NM_001197104	tophat
KMT2A	13H150	PTD	chr11:118339489	NA	NM_001197104	tophat
KMT2A	06H016	PTD	chr11:118342376	NA	NM_001197104	tophat
KMT2A	09H045	PTD	chr11:118342376	NA	NM_001197104	tophat
KMT2A	07H034	R3659Q	chr11:118380738	0.4015	NM_001197104	casava
KMT2C	11H132	R3995fsX	chr7:151851507	0.2482	NM_170606	casava
KMT2C	12H067	E1165K	chr7:151919092	0.3261	NM_170606	casava
KMT2D	03H090	G5075R	chr12:49420526	0.4574	NM_003482	casava
KRAS	11H017	G12D	chr12:25398284	0.5272	NM_004985	kmer

NF1	08H018	W223R	chr17:29508740	0.2642	NM_000267	casava
NF1	11H145	T676fsX	chr17:29553477	0.8333	NM_000267	casava
NF1	13H056	R1748X	chr17:29654553	0.8438	NM_000267	casava
NF1	06H075	A1852S	chr17:29657321	0.8222	NM_000267	casava
NF1	10H174	R2237X	chr17:29665110	0.5714	NM_000267	casava
NF1	13H018	R2616X	chr17:29684326	0.5455	NM_000267	casava
NPM1	02H026	L287fs (insTCTG)	chr5:170837543	0.4162	NM_002520	casava
NPM1	06H074	W288fs (ins CAGA)	chr5:170837547	0.412	NM_002520	casava
NRAS	11H140	Y64D	chr1:115256521	0.4776	NM_002524	kmer
NRAS	12H170	Q61H	chr1:115256528	0.0753	NM_002524	kmer
NRAS	05H180	Q61H	chr1:115256528	0.3292	NM_002524	kmer
NRAS	04H101	Q61R	chr1:115256529	0.3051	NM_002524	kmer
NRAS	12H055	Q61K	chr1:115256530	0.3464	NM_002524	kmer
NRAS	09H045	G13D	chr1:115258744	0.4461	NM_002524	kmer
NRAS	12H170	G12D	chr1:115258747	0.05	NM_002524	kmer
NRAS	10H051	G12V	chr1:115258747	0.0596	NM_002524	kmer
NRAS	11H145	G12D	chr1:115258747	0.0686	NM_002524	kmer
NRAS	03H094	G12S	chr1:115258748	0.0669	NM_002524	kmer
PTPN11	12H067	G60V	chr12:112888163	0.3742	NM_002834	kmer
PTPN11	11H017	G60V	chr12:112888163	0.1391	NM_002834	kmer
PTPN11	11H177	E69K	chr12:112888189	0.2018	NM_002834	kmer
PTPN11	06H029	A72T	chr12:112888198	0.5011	NM_002834	kmer
PTPN11	11H044	S502P	chr12:112926884	0.4058	NM_002834	casava
RUNX1	11H170	R207W	chr21:36206893	0.4	NM_001754	casava
RUNX1	12H106	T181K	chr21:36231842	0.4885	NM_001754	casava
RUNX1	05H180	R166fsX	chr21:36252864	0.4821	NM_001754	casava
RUNX1	08H022	R162S	chr21:36252876	0.5303	NM_001754	casava
RUNX1	11H170	V130F	chr21:36252974	0.5	NM_001754	casava
RUNX1	03H030	K110Q	chr21:36259163	0.9858	NM_001754	casava
RUNX1	11H140	Q15fsX	chr21:36421151	0.4771	NM_001754	casava
SETBP1	04H132	T228fsX	chr18:42456670	0.3488	NM_001130110	casava
SETBP1	09H057	D868Y	chr18:42531907	0.4932	NM_015559	casava
SMC1A	13H141	R785P	chrX:53430498	0.9057	NM_001281463	casava
SPI1	12H055	R171H	chr11:47377079	0.5027	NM_003120	casava
SRSF2	09H057	P95H	chr17:74732959	0.6141	NM_003016	kmer
SRSF2	11H140	P95L	chr17:74732959	0.5151	NM_003016	kmer
SRSF2	08H054	P95H	chr17:74732959	0.4683	NM_003016	kmer
STAG2	11H140	L566fsX	chrX:123196809	0.1411	NM_001042751	casava
STAG2	03H030	L571P	chrX:123196825	0.8176	NM_001042751	casava
TET2	12H170	G563fsX	chr4:106156785	0.575	NM_001127208	casava
TET2	12H058	E628X	chr4:106156981	0.5045	NM_001127208	casava
TET2	07H038	Q705X	chr4:106157212	0.4236	NM_001127208	casava
TET2	11H140	A991fsX	chr4:106158069	0.4379	NM_001127208	casava
TET2	12H012	L1258fsX	chr4:106164905	0.3692	NM_001127208	casava
TET2	02H026	C1273S	chr4:106180789	0.5	NM_001127208	casava
TET2	12H067	G1860fsX	chr4:106197244	0.7419	NM_001127208	casava
U2AF1	11H132	Q157P	chr21:44514777	0.3876	NM_006758	kmer
U2AF1	10H113	R156H	chr21:44514780	0.3608	NM_006758	kmer

U2AF1	13H141	S34F	chr21:44524456	0.4968	NM_006758	kmer
U2AF1	10H078	S34F	chr21:44524456	0.4759	NM_006758	kmer
ZBTB7A	03H028	T29P	chr19:4055146	0.8537	NM_015898	casava

**TABLE S4**

Mutated gene	p-value	Odds
TP53	4.0E-31	56.62080152
NPM1	1.8E-09	0.055403543
FLT3	2.5E-09	0.10713596
DNMT3A	0.004	0.34436868
KIT	0.008	0
CALR	0.015	15.80128752
WT1	0.021	0
NF1	0.023	3.618548486
IDH2	0.040	0.302616828
ASXL1	0.063	0.262347861
KRAS	0.064	0.177323639
IDH1	0.065	0.170461615
SETBP1	0.071	10.38924998
JAK2	0.088	3.024684649
GATA2	0.139	0
BCOR	0.139	0
CEBPA (biallelic)	0.140	0
EVI1.r	0.229	0
RAD21	0.366	0
SF3B1	0.379	0
TET2	0.445	0.666636145
SRSF2	0.447	0.570485401
U2AF1	0.498	1.60365777
ZBTB7A	0.513	1.708820227
SPI1	0.513	1.708820227
STAG2	0.550	0.523800401
KMT2A	0.581	1.296740197
NRAS	0.590	0.760567794
CREBBP	0.593	1.279026452
ETV6	0.595	0
SMC3	0.595	0
ASXL2	0.605	0
IKZF1	0.605	0
KMT2C	0.623	1.719556397
CBL	0.623	1.719556397
CSF3R	0.623	1.719556397
RUNX1	0.675	0.722794981
PTPN11	0.788	1.17192757
ZRSR2	1.000	0
PHF6	1.000	0
KMT2D	1.000	0.633065818
SMC1A	1.000	0.503653693
CEBPA (monoallelic)	1.000	0.503653693
EZH2	1.000	1.021161766

TABLE S5

Compound	Compound name	Company	Catalog #	Description
UM0022485	UM0022485 from UdeM	UdeM		
UM0042538	Cytarabine	TOCRIS	4520	Antimetabolite - pyrimidine analogue
UM0092374	SPECS_AE-848/11419066	SPECS	AE-848/11419066	
UM0092376	SPECS_AE-848/11419104	SPECS	AE-848/11419104	
UM0092618	SPECS_AE-848/32006058	SPECS	AE-848/32006058	
UM0093235	SPECS_AF-399/15335038	SPECS	AF-399/15335038	
UM0093450	SPECS_AF-399/40684392	SPECS	AF-399/40684392	
UM0093569	UM0093569 from UdeM	UdeM		
UM0093662	SPECS_AF-399/40960315	SPECS	AF-399/40960315	
UM0093794	SPECS_AG-205/07907018	SPECS	AG-205/07907018	
UM0093796	SPECS_AG-205/07932038	SPECS	AG-205/07932038	
	1,2,2-trimethylpropyl 4-(2-ethoxyphenyl)-6-methyl-2-oxo-			
UM0094058	1,2,3,4-tetrahydro-5-	Chembridge	5612329	
UM0094107	SPECS_AG-205/12013023	SPECS	AG-205/12013023	
UM0094890	SPECS_AG-205/36915225	SPECS	AG-205/36915225	
UM0095749	SPECS_AG-650/41069260	SPECS	AG-650/41069260	
UM0096165	SPECS_AG-670/41019315	SPECS	AG-670/41019315	
UM0096176	SPECS_AG-690/08355059	SPECS	AG-690/08355059	
UM0096705	UM0096705 from UdeM	UdeM		
UM0096781	UM0096781 from UdeM	UdeM		
UM0097793	SPECS_AG-690/15441703	SPECS	AG-690/15441703	
UM0098860	SPECS_AH-487/15276024	SPECS	AH-487/15276024	
UM0098937	SPECS_AH-487/40669985	SPECS	AH-487/40669985	
UM0099317	UM0099317 from UdeM	UdeM		
UM0099733	SPECS_AK-777/37037051	SPECS	AK-777/37037051	
UM0099775	SPECS_AK-778/11708035	SPECS	AK-778/11708035	
UM0100383	SPECS_AK-968/11841778	SPECS	AK-968/11841778	
	1-(2-bromobenzyl)-4-(3,4,5-trimethoxybenzyl)piperazine	Chembridge	5865602	
UM0101184	SPECS_AK-968/15253444	SPECS	AK-968/15253444	
UM0101480	SPECS_AK-968/15364033	SPECS	AK-968/15364033	
UM0101838	SPECS_AK-968/37005200	SPECS	AK-968/37005200	
UM0101845	SPECS_AK-968/37005263	SPECS	AK-968/37005263	
UM0101847	SPECS_AK-968/37005284	SPECS	AK-968/37005284	
UM0102603	SPECS_AK-968/41017746	SPECS	AK-968/41017746	
UM0102657		Chembridge	8803078	
UM0102836	SPECS_AK-968/41022109	SPECS	AK-968/41022109	
UM0103032	UM0103032 from UdeM	UdeM		
UM0103728	SPECS_AM-807/14959586	SPECS	AM-807/14959586	
UM0104715	SPECS_AN-648/40682639	SPECS	AN-648/40682639	
UM0104768	SPECS_AN-648/40925375	SPECS	AN-648/40925375	
UM0105063	SPECS_AN-698/40705204	SPECS	AN-698/40705204	
UM0105101	SPECS_AN-698/40745478	SPECS	AN-698/40745478	
	N-[4-(1,3-benzoxazol-2-yl)phenyl]cyclopropanecarboxamid	Chembridge	7070640	
UM0105621				
UM0105815	SPECS_AN-988/40875350	SPECS	AN-988/40875350	
UM0106743	UM0106743 from UdeM	UdeM		
UM0106805	SPECS_AO-990/15068023	SPECS	AO-990/15068023	
UM0106825	UM0106825 from UdeM	UdeM		
UM0107130	SPECS_AP-906/41650452	SPECS	AP-906/41650452	
UM0107165	UM0107165 from UdeM	UdeM	20 mM stock, small vol	
UM0118129	Cloperastine hydrochloride	Santa Cruz Biotech	sc-234405	Antihistaminic
UM0118172	Sulfamethoxy pyridazine	Sigma	S7257	Antibacterial
	Proadifen hydrochloride (SKF 525A (hydrochloride))	Cayman chemical	15040	Cytochrome P (CYP)450 inhibitor
UM0118177				
UM0118216	Dibucaine	Santa Cruz Biotech	sc-252684	Local anesthetic
UM0118223	Simvastatin	Abcam	ab120505	HMG-CoA reductase inhibitor
UM0118262	Etoposide	TOCRIS	1226	DNA topoisomerase II inhibitor
UM0118264	Fenbendazole	Sigma	F5396	Antiparasitic
UM0118273	Flunisolide	Sigma	F5021	Corticosteroid
UM0118279	Flumethasone	Sigma	F9507	Corticosteroid
UM0118313	Hydrocortisone base	Sigma	H4001	Cortisol
UM0118357	N6-methyladenosine	Selleckchem	S3190	Base modified analogue of adenosine

UM0118535	Ifenprodil tartrate	Santa Cruz Biotech	SC-295173	NMDA receptor antagonist
UM0118582	CLEMASTINE	Cayman chemical	14637	Antihistaminic and anticholinergic
UM0118601	Betamethasone	Santa Cruz Biotech	SC-204647	Glucocorticoid
UM0118604	Amiodarone hydrochloride	Cayman chemical	15213	class III antiarrhythmic agent
UM0118623	Cyclosporin A	Cayman chemical	12088	Immunosuppressant drug
UM0118638	Carbetapentane citrate	Santa Cruz Biotech	SC-203538	Non-opioid antitussive and anticonvulsant agent
UM0118693	Terconazole	Sigma	SMB00286	Antifungal agent
UM0118717	Budesonide	Cayman chemical	15407	Glucocorticoid
UM0118731	Pentamidine isethionate	Santa Cruz Biotech	sc-204176	Antimicrobial
UM0118772	Dacarbazine	Sigma	D2390	Alkylating agent
UM0118790	Mometasone furoate	Sigma	M4074	Glucocorticoid
UM0118805	Azacytidine-5	TOCRIS	3842	DNA methyltransferase inhibitor
UM0118859	Raloxifene hydrochloride	Cayman chemical	10011620	ER ligand
UM0118868	Pramoxine hydrochloride	Santa Cruz Biotech	sc-264141	Topical anesthetic
UM0118887	Flurandrenolide	Sigma	F1642	Corticosteroid
UM0118891	Halcinonide	Carbosynth	FH23727	Corticosteroid
UM0118901	Atovaquone	Sigma	A7986	Antiprotozoal and Antimalarial
UM0118984	Methiazole	Accuratechemical	TXL6214-100	Antithyroid agent
UM0118995	S(-)Etidopride hydrochloride	Sigma	E101	D2 dopamine receptor antagonist
UM0119063	Methacycline hydrochloride	Selleck	S2527	Tetracycline antibiotic
UM0119088	Piperacetazine	Sigma	PH004722	Antipsychotic drug
UM0119104	Ribavirin	TOCRIS	4501	Anti-viral drug
UM0119120	Trifluridine	Selleck	S1778	Anti-herpesvirus drug
UM0119143	ARTESUNATE	Cayman chemical	11817	Pro-drug anti-malaria
UM0119195	LAPACHONE, beta-	Abcam	ab141097	Topoisomerase-inhibitor
UM0119205	PROSTAGLANDIN E2	Cayman chemical	14010	Active lipid compound (hormone-like effects)
UM0119219	RAPAMYCIN	Cayman chemical	13346	IL-2 and mTOR Complex 1 inhibitor
UM0119222	SHIKONIN	Cayman chemical	14751	Pyruvate kinase M2 inhibitor
UM0119258	DIACETYLKORSEVERILINE	Affix Scientific	AF3185	Antiarrhythmic
UM0119268	GENISTIN	Cayman chemical	14174	Phytoestrogen
UM0119334	PATULIN	Cayman chemical	11346	Mycotoxin
UM0119434	RUBESCENSIN A	LKT Laboratories Inc	R8206	Diterpene originally found in Rabdosia
UM0119467	CHARTREUSIN	LKT Laboratories Inc	C2803-5mg	Antibiotic
UM0119502	Aminopterin	ENZO Life Sciences	ALX-440-041-M050	Dihydrofolate reductase inhibitor
UM0119612	Bay 11-7085	Cayman chemical	14795	I $\kappa$ B $\alpha$ phosphorylation inhibitor (NF-kb pathway)
UM0119621	Benztropine mesylate	Sigma	SML0847	Muscarinic antagonist
UM0119648	Cyclophosphamide	TOCRIS	4091	Alkylating agent
UM0119657	(+)-Chlorpheniramine maleate	Sigma	C3025	H1 Histamine receptor antagonist
UM0119662	Calmidazolium chloride	TOCRIS	2561	Calmodulin antagonist
UM0119682	7-Chloro-4-hydroxy-2-phenyl-1,8-naphthyridine	Santa Cruz Biotech	sc-300073	Adenosine A1-R antagonist
UM0119688	Cantharidic Acid	Abcam	ab141725	PP2A and PP1 inhibitor
UM0119703	2',3'-dideohydro-3'-deoxythymidine 4'-Chloro-3-alpha-	Sigma	D1413	Nucleoside analogue. HIV replication inhibitor.
UM0119707	(diphenylmethoxy)tropane		917	Dopamine transporter inhibitor
UM0119718	Dihydroergotamine	Santa Cruz Biotech	sc-294343	Serotonin antagonist and vasoconstrictor
UM0119800	Eliprodiol	Sigma	E2031	NMDA antagonist drug
UM0119883	hydroxyurea	Sigma	H8627	Ribonucleotide reductase inhibitor. Antineoplastic
UM0119908	NSC 95397	calbiochem	217694	Cdc25 inhibitor
UM0119968	L-687,384 hydrochloride	Sigma	L8539-5MG	$\alpha$ 1 receptor agonist
UM0119978	6-Methyl-2-(phenylethynyl)pyridine		M5435-5MG	mGluR5 metabotropic glutamate receptor antagonist
UM0119979	2-methoxyestradiol	Sigma	M6383-5MG	Natural metabolite of estradiol
UM0119998	MG 624	TOCRIS	1356	$\alpha$ 7 nACh receptor antagonist
UM0120016	L-745,870 hydrochloride	TOCRIS	1002	D $_4$ dopamine receptor antagonist
UM0120130	SU 6656	Cayman chemical	13338	Src kinases inhibitor
UM0120205	SKF 96365	Cayman chemical	10009312	SOCE inhibitor
UM0120206	Salmeterol xinafoate	Cayman chemical	16009	$\beta$ -adrenergic agonist
UM0120219	DL-Stearoylcarnitine chloride	io Technology (Ced)	S-126-5	
UM0120224	SU 4312	Enzo life sciences	BML-EI306-0005	VEGFR inhibitor
UM0120269	Suramin hexasodium	Enzo life sciences	ALX-430-022-M050	Purinergic receptor inhibitor
UM0120298	WAY-100635 maleate	Cayman chemical	14599	Serotonin 5-HT1A receptor antagonist
UM0120299	YC-1	ENZO Life Sciences	ALX-420-025-M005	Guanylyl cyclase activator
UM0120317	(+)-trans-(1R,2R)-U-50488	Biotrend	BN0526	K opioid agonist
UM0120474	UM0120474 from UdeM	UdeM		
UM0120482	6 $\alpha$ -METHYLPREDNISOLONE	Cayman chemical	11800	Glucocorticoid
UM0120587	methylmethane sulfonate	Sigma	129925-5G	Alkylating agent
UM0120625	FORMESTANE	Selleck	S2208	Aromatase inhibitor

UM0120639	HOMIDIUM BROMIDE	Sigma	E7637-1G	DNA intercalating
UM0120732	UM0120732 from UdeM	UdeM		
UM0120832	CHOLEST-5-EN-3-ONE	Sigma	C75004-500 mg	Cholesterol metabolism
UM0120854	LANOSTEROL	Sigma	L5768	Cholesterol precursor sterol
UM0121014	5alpha-CHOLESTAN-3beta-OL-6-ONE (6-Ketocholestanol)	Santa Cruz Biotech	sc-210525A	Oxygenated cholesterol compound
UM0121035	7-OXOCHOLESTEROL	Sigma	C2394	Cholesterol metabolism
UM0121111	alpha-MANGOSTIN	Sigma	M3824-10 mg	Antioxidant and anti-inflammatory
UM0121120	COSMOSIIN HEXAACETATE:	AvaChem Scientific	2905	Flavonoid
UM0121249	AMINACRINE	Selleck	S4303	Topical antiseptic
UM0121301	EZETIMIBE	AdooQ Bioscience	A10379	Inhibitor of cholesterol absorption
UM0121349	EDOXUDINE	into Research Chem	E915020	Thymidine analogue
UM0121357	ESTRADIOL CYPIONATE	Santa Cruz Biotech	sc-234874	Prodrug of estradiol
UM0121415	FLUMETHAZONE PIVALATE	Sigma	F0891-100 mg	Glucocorticoid receptor agonist
UM0121425	DEXAMETHASONE	Sigma	D4902-25MG	Glucocorticoid
UM0121443	FLUDROCORTISONE ACETATE	AstaTech	35746	Corticosteroid
UM0121463	BETAMETHASONE VALERATE	AdooQ Bioscience	A10131	Glucocorticoid
UM0121469	HYDROXYPROGESTERONE	Abcam	ab142640	Synthetic progestational agent
UM0121477	HYDROXYZINE PAMOATE	Sigma	H9010-10G	Antihistaminic
UM0121509	E-64-C	Cayman chemical	10007964	Cystein protease inhibitor
UM0121517	MYCOPHENOLIC ACID	Abcam	ab120664	Immunosuppressant
UM0123617	UM0123617 from UdeM	UdeM		
UM0125497	UM0125497 from UdeM	UdeM		
UM0125633	UM0125633 from UdeM	UdeM		
UM0125695	UM0125695 from UdeM	UdeM		
UM0125748	UM0125748 from UdeM	UdeM		
UM0125807	UM0125807 from UdeM	UdeM		
UM0126171	UM0126171 from UdeM	UdeM		
UM0126248	UM0126248 from UdeM	UdeM		
UM0126615	UM0126615 from UdeM	UdeM		
UM0127622	UM0127622 from UdeM	UdeM		
UM0127808	Triciribine AKT inhibitor V	Selleckchem.	S1117	Akt inhibitor
UM0127831	Ryuvidine	Tocris	2609	SETD8 and cdk4 inhibitor
UM0127846	EGFR Inhibitor	Calbiochem	324674-1MG	EGFR Inhibitor
UM0127851	Fascaplysin, Synthetic	AG Scientific	F-1136	Cdk4/D1 inhibitor
UM0127854	Flt-3 Inhibitor III	calbiochem	343022-5MG	FLT3 inhibitor
UM0127866	GTP-14564	Tocris	2086	Class III receptor tyrosine kinase inhibitor
UM0127891	MK2a Inhibitor	Santa Cruz Biotech	sc-203138	MK2a Inhibitor
UM0127902	PKD1/Akt/Flt Dual Pathway	calbiochem	521275-5MG	PKD1/Akt inhibitor
UM0127927	SU11652	ENZO Life Sciences	BML-EI408-0001	VEGFR inhibitor
UM0127943	Dasatinib	Adooq Bioscience	A10290	BCR/ABL and Src family tyrosine kinase inhibitor
UM0127945	Gefitinib	Selleckchem.	S1025	EGFR Inhibitor
UM0127950	Sorafenib (Nexavar)	Adooq Bioscience	A10001-5	Tyrosine protein kinase inhibitor
UM0127952	Imatinib mesylate	Adooq Bioscience	A10468	Tyrosine protein kinase inhibitor
UM0127955	Mubritinib	Selleckchem.	S2216	HER2/ErbB2 inhibitor
UM0128550	Vorinostat (SAHA)	Adooq Bioscience	A10979	HDAC inhibitor
UM0128557	M-344	Cayman chemical	13174	HDAC inhibitor
UM0128576	NSC-3852	Santa Cruz Biotech	sc-205773	HDAC inhibitor
UM0129937	EPZ6438	MedChem Express	HY13803	EZH2 inhibitor
UM0129939	UNC0646			G9a and GLP HMTases inhibitor
UM0130968	Selumetinib/AZD6244	Selleckchem.	S1008	MEK1 inhibitor
UM0130977	Trametinib	Adooq Bioscience	A11029	MEK1 and MEK2 inhibitor Immunomodulator, anti-inflammatory, anti-angiogenic activity
UM0130980	Lenalidomide	Adooq Bioscience	A10522	activity
UM0130989	Quizartinib (AC220)	Adooq Bioscience	A10027	FLT3 inhibitor
UM0131000	FGF/VEGF Receptor Tyrosine Kinase Inhibitor (PD173074)	Santa Cruz Biotechnol	sc-202610A	FGF and VEGF inhibitor
UM0131001	Ki8751	Adooq Bioscience	A10502-10	VEGFR-2 inhibitor
UM0131002	PDGFR Tyrosine Kinase Inhibitor	Calbiochem	521237-5MG	PDGFR Tyrosine Kinase Inhibitor
UM0131006	Flt3 Inhibitor IV	Santa Cruz Biotechnol	sc-221615	FLT3 inhibitor
UM0131011	c-Met/RON Dual Kinase Inhibitor	Calbiochem	448104-5MG	c-Met/RON kinase inhibitor
UM0131110	from UdeM	UdeM		
UM0132260	Pitavastatin	UdeM		Statins
UM0132676	Daunorubicin	TOCRIS	1467	Anthracycline - DNA intercalating
UM0133724	5FU	TOCRIS	3257	Antimetabolite
UM0133752	All-trans retinoic acid (Vesanoid, Tretinoin)	TOCRIS	695	Endogenous agonist for retinoic acid receptors
UM0134798	Prednisolone	Cayman chemical	15933	Glucocorticoid

UM0135480	Atorvastatin	Abcam	ab141083	Statins
UM0135478	Volasertib (BI6727)	Selleckchem.	S2235	PLK1 inhibitor
UM0135479	Rigosertib (ON-01910)	Selleckchem.	S1362	PLK1 inhibitor
UM0135481	Midostaurin (PKC412)	Adooq Bioscience	A12650	Protein kinase inhibitor
UM0135482	EPZ5676	Adooq Bioscience	A12735	DOT1L inhibitor
UM0135483	Bortezomid (Velcade)	Adooq Bioscience	A10160	Proteasome inhibitor
UM0135484	Temsirolimus (CCI-779)	Adooq Bioscience	A10906	mTOR inhibitor
UM0135485	Tipifarnib	Adooq Bioscience	A10935	Farnesyltransferase inhibitor
UM0135486	AZD1152 (Barasertib)	Adooq Bioscience	A10109	Aurora B kinase inhibitor
UM0135487	Alisertib (MLN8237)	Adooq Bioscience	A10004	Aurora A kinase inhibitor
UM0135488	Vismodegib (RO5450815)	Adooq Bioscience	A10258	Hedgehog signalling pathway antagonist
UM0135489	MLN4924	Adooq Bioscience	A11260	NAE inhibitor
UM0135490	AZD1208	Adooq Bioscience	A13203	PIM kinase inhibitor
UM0135491	17-AAG (tanespimicin )	Adooq Bioscience	A10010	HSP90 inhibitor
UM0135492	STA-9090 (ganetespib)	Adooq Bioscience	A11402	HSP90 inhibitor
UM0135493	AZD-2014	Adooq Bioscience	A11303	mTOR inhibitor
UM0135494	AZD-8055	Adooq Bioscience	A10114	mTOR inhibitor
UM0135495	MK-2206, AKT inhibitor	Adooq Bioscience	A10003	Akt inhibitor
UM0135496	Alvocidib (flavopiridol)	Adooq Bioscience	A10390	Cdk9 kinase inhibitor
UM0135497	ABT-199	Adooq Bioscience	A12500	Bcl-2 inhibitor
UM0135498	Mitoxantrone	Cayman Chemicals	14842	Topoisomerase II inhibitor
UM0135499	BET151 (GSK1210151A)	ChemieTek	I-BET151	BET inhibitor for BRD2, BRD3 and BRD4
UM0135500	Voreloxin hydrochloride	MedChem Express	HY-16518	Anthracenedione - Topoisomerase II inhibitor
UM0135501	SB590885	Selleckchem.	S2220	B-Raf inhibitor
UM0135502	Lonafarnib	Selleckchem.	S2797	Farnesyltransferase inhibitor
UM0135503	Selinexor (KPT-330)	Selleckchem.	S7252	CRM1 inhibitor
UM0135504	PF-3758309	Selleckchem.	S7094	PAK4 inhibitor
UM0135505	CPI-613	SIGMA	SML0404	$\alpha$ -ketoglutarate dehydrogenase inhibitor
UM0135506	Arsenic trioxide (Trisenox, As <sub>2</sub> O <sub>3</sub> )	SIGMA	A1010	Arsenic oxide
UM0135507	6-Mercaptopurine	TOCRIS	4103	Antimetabolite - Purine analogue
UM0135508	Clofarabine	TOCRIS	2600	Antimetabolite - Purine nucleoside
UM0135509	Temozolomide	TOCRIS	2706	Alkylating agent
UM0135510	Thioridazine hydrochloride	TOCRIS	3070	Dopamine receptor antagonist
UM0135511	Panobinostat	Selleckchem.	LBH589	HDAC inhibitor
UM0135578	GSK126	ActiveBiochem	A1275	EZH2 inhibitor
UM0135579	UNC2400	TOCRIS	4905	EZH2 inhibitor
UM0135581	UNC1999	TOCRIS	4904	EZH1/2 inhibitor
UM0135583	Fludarabine	TOCRIS	3495	Antimetabolite - Purine analogue
UM0135584	Mitomycin C	Sigma	10107409001-2mg	Antibiotic
UM0135585	Topotecan hydrochloride hydrate	Sigma	T2705-10MG	Topoisomerase I-inhibitor
UM0135586	gemcitabine	Selleckchem	S1714-50mg	Antimetabolite - Nucleoside analogue
UM0135587	Ruxolitinib	Selleckchem	S1378-5mg	JAK1/2 inhibitor
UM0135618	UM0135618 from UdeM	UdeM		
UM0135680	UM0135680 from UdeM	UdeM		
UM0135681	Cerivastatin	UdeM		Statins



**TABLE S6**

Group	BCLQ ID	Karyotype	TP53	RAS	JAK2	FLT3	age	sex	Status at sampling	FAB	WBC (x 10 <sup>9</sup> /L)	Tissue	Blast %
CK	03H030	Complex	WT	WT* (Low NF1)	V617F	WT	82	F	Diagnosis	AML-M0	34	Blood	60
CK	03H090	Complex	WT	WT	WT	ITD	63	F	Diagnosis	AML-M1	109.7	Blood	90
CK	03H094	Complex	Altered	NRAS G12S	WT	WT	56	M	Relapse	AML-M1	85.4	Blood	90
CK	04H132	Complex	WT	WT* (Low NF1)	WT	D835H (VAF8%)	46	M	Diagnosis	AML-M4	161	Blood	48
CK	05H180	Complex	WT	NRAS Q61H	WT	WT	70	M	Diagnosis	AML-M2	200.8	Blood	35
CK	06H004	Complex	Altered	WT* (Low NF1)	WT	WT	59	F	Diagnosis	Not classifiable by FAB criteria	321	Bone marrow	44
CK	06H016	Complex	WT	WT* (Low NF1)	WT	WT	69	F	post-treatment	AML-M5A	48.4	Bone marrow	87
CK	07H038	Complex	WT	BRAF R575K*	WT	WT	66	M	Diagnosis	AML-M0	9.2	Blood	90
CK	07H148	Complex	Altered	WT	WT	WT	68	F	Diagnosis	AML-M2	27	Bone marrow	26
CK	07H156	Complex	Altered	WT	WT	ITD (VAF 11%)	62	M	Diagnosis	AML-M2	49	Bone marrow	44
CK	09H054	Complex	WT	WT	V617F	WT	54	F	Diagnosis	Not classifiable by FAB criteria	80.3	Blood	63
CK	09H057	Complex	Altered	WT	WT	WT	62	M	Diagnosis	Not classifiable by FAB criteria	31.4	Blood	60
CK	09H078	Complex	Altered	WT	WT	WT	58	F	Diagnosis	AML-M1	4.7	Bone marrow	34
CK	09H084	Complex	Altered	WT	WT	WT	68	F	Diagnosis	Not classifiable by FAB criteria	48.7	Bone marrow	40
CK	09H085	Complex	WT	WT	V617F	WT	72	F	Diagnosis	AML-M7	35.9	Blood	65
CK	10H014	Complex	Altered	WT	WT	WT	77	M	Diagnosis	AML-M0	1.3	Bone marrow	72
CK	10H034	Complex	WT	WT	WT	WT	65	M	Diagnosis	AML-M2	15.1	Blood	38
CK	10H066	Complex	Altered	WT* (Low NF1)	WT	WT	54	M	Relapse	AML-M6	14.1	Blood	28
CK	10H070	Complex	Altered	WT* (Low NF1)	WT	ITD	63	F	Relapse	AML-M1	20.4	Blood	95
CK	10H087	Complex	Altered	WT	WT	WT	73	M	Diagnosis	AML-M1	13.3	Blood	60
CK	10H174	Complex	Altered	NF1 R2237X (Low NF1)	WT	WT	59	F	Diagnosis	AML-M4	112.7	Bone marrow	70
CK	11H002	Complex	Altered	WT	WT	WT	65	M	post-treatment	AML-M0	18.1	Bone marrow	80
CK	11H017	Complex	WT	KRAS G12D, PTPN11 G60V	WT	WT	35	M	Diagnosis	Not classifiable by FAB criteria	20.3	Bone marrow	56
CK	11H170	Complex	WT	WT	WT	WT	51	F	Diagnosis	AML-M0	50.5	Blood	94
CK	12H096	Complex	WT	WT	WT	WT	68	F	Diagnosis	AML-M5	28.4	Blood	66
CK	12H106	Complex	Altered	WT	WT	WT	67	M	Diagnosis	Not classifiable by FAB criteria	166.8	Blood	87
CK	13H107	Complex	WT	WT	WT	WT	59	M	Relapse	Not classifiable by FAB criteria	11.7	Blood	70
Inter	03H033	Normal Karyotype	WT	NRAS S17N	WT	ITD	47	F	Relapse	AML-M1	180.5	Blood	95
Inter	05H143	Normal Karyotype	WT	NRAS G12D	WT	ITD	50	M	Relapse	AML-M5A	126.4	Blood	85
Inter	07H005	Normal Karyotype	WT	WT	WT	ITD	46	F	Diagnosis	Not classifiable by FAB criteria	64	Blood	85
Inter	07H112	Normal Karyotype	WT	NRAS Q61H	WT	WT	49	F	Relapse	AML-M1	34.2	Blood	81
Inter	11H010	Normal Karyotype	WT	WT	WT	ITD	69	F	Relapse	AML-M1	127	Blood	95
Inter	11H046	Normal Karyotype	WT	WT	V617F	WT	77	M	Diagnosis	AML-M0	48.8	Blood	80
Inter	11H095	Normal Karyotype	WT	KRAS G12V	WT	WT	50	M	Diagnosis	AML-M5A	1.4	Bone marrow	87
Inter	11H138	Intermediate risk (abn	WT	WT	WT	ITD	71	M	Diagnosis	AML-M0	24	Bone marrow	94
Inter	11H186	Normal Karyotype	WT	WT	WT	ITD	27	F	Relapse	AML-M1	53.3	Bone marrow	82
Inter	12H195	Normal Karyotype	WT	PTPN11 G603E	WT	ITD	57	F	Relapse	AML-M4	34.1	Blood	54
Inter	13H114	Normal Karyotype	WT	WT	WT	ITD	58	M	Diagnosis	Not classifiable by FAB criteria	68.4	Bone marrow	83

**TABLE S7**

Compound	Compound name	CK (log <sub>2</sub> (median IC <sub>50</sub> ))	Inter (log <sub>2</sub> (median IC <sub>50</sub> ))	p.value
UM0119502	Aminopterin	2.00	2.00	0.38255
UM0135586	gemcitabine	2.00	2.00	0.19397
UM0135498	Mitoxantrone	2.34	2.00	0.01956
UM0135511	Panobinostat	2.60	2.00	0.01638
UM0135483	Bortezomid (Velcade)	2.66	2.59	0.83005
UM0135504	PF-3758309	2.72	2.00	0.54986
UM0135478	Volasertib (BI6727)	2.72	2.59	0.68806
UM0132676	Daunorubicin	2.79	2.00	0.00372
UM0135479	Rigosertib (ON-01910)	3.09	5.84	0.00350
UM0135492	STA-9090 (ganetespib)	3.11	2.58	0.01939
UM0135508	Clofarabine	3.26	2.27	0.00309
UM0135585	Topotecan hydrochloride hydrate	3.52	2.00	0.03553
UM0130977	Trametinib	4.18	2.00	0.00864
UM0135681	Cerivastatin from chemists	4.97	4.89	0.79674
UM0135486	AZD1152 (Barasertib)	5.52	4.66	0.25991
UM0042538	Cytarabine	5.59	3.75	0.09737
UM0135494	AZD-8055	5.72	7.05	0.15201
UM0135503	Selinexor (KPT-330)	6.01	5.61	0.25072
UM0135507	6-Mercaptopurine	6.14	6.72	0.37296
UM0135584	Mitomycin C	6.44	5.67	0.00244
UM0135487	Alisertib (MLN8237)	6.73	6.44	0.94864
UM0135496	Alvocidib (flavopiridol)	6.77	5.83	0.00000
UM0127927	SU11652	6.86	5.07	0.15669
UM0135500	Voreloxin hydrochloride	7.02	5.69	0.00244
UM0127846	EGFR Inhibitor	7.13	7.54	0.14748
UM0135489	MLN4924	7.78	8.54	0.07647
UM0135491	17-AAG (tanespimicin )	7.97	7.43	0.09454
UM0127943	Dasatinib	7.98	5.41	0.25983
UM0127851	Fascaplysin, Synthetic	8.00	8.01	0.65696
UM0135493	AZD-2014	8.01	8.52	0.22740
UM0128576	NSC-3852	8.06	7.39	0.10832
UM0127854	FIt-3 Inhibitor III	8.25	7.98	0.82440
UM0127808	Triciribine AKT inhibitor V	8.60	8.39	0.94946
UM0118772	Dacarbazine	8.62	8.97	0.29293
UM0135481	Midostaurin (PKC412)	8.72	8.52	0.84917
UM0132260	Pitavastatin	8.72	8.15	0.25072
	4'-Chloro-3- $\alpha$ -(diphenylmethoxy)tropane			
UM0119707	hydrochloride	8.87	9.99	0.10405
UM0119998	MG 624	9.05	8.14	0.46486
UM0135583	Fludarabine	9.06	7.93	0.00030
UM0135587	Ruxolitinib	9.06	8.94	0.38456
UM0130989	Quizartinib (AC220)	9.06	6.93	0.05333
	5 $\alpha$ -CHOLESTAN-3 $\beta$ -OL-6-ONE (6-			
UM0121014	Ketocholestanol)	9.15	9.64	0.11577
UM0118262	Etoposide	9.27	8.12	0.00442
UM0127902	PK1/Akt/FIt Dual Pathway Inhibitor	9.47	8.77	0.02704
UM0119120	Trifluridine	9.60	9.97	0.25983
UM0128550	Vorinostat (SAHA)	9.61	8.83	0.07109

UM0119219	RAPAMYCIN	9.66	13.29	0.26259
UM0128557	M-344	9.72	8.90	0.02262
UM0121349	EDOXUDINE	9.76	10.28	0.41088
UM0135499	BET151 (GSK1210151A)	9.80	10.15	0.67562
UM0119222	SHIKONIN	10.03	9.66	0.58951
UM0118264	Fenbendazole	10.08	10.22	0.10752
UM0118859	Raloxifene hydrochloride	10.25	11.97	0.10061
UM0118535	Ifenprodil tartrate	10.33	10.69	0.07146
UM0127831	Ryuvidine	10.41	10.00	0.03805
UM0118984	Methiazole	10.44	11.04	0.00223
UM0135480	Atorvastatin	10.45	9.58	0.09454
UM0135618	Statine From Chemist (Pf)	10.50	9.79	0.58417
UM0131001	Ki8751	10.50	9.33	0.24646
UM0125497	UM0125497 from UdeM	10.56	11.12	0.20114
UM0135502	Lonafarnib	10.59	10.72	0.64052
UM0092374	SPECS_AE-848/11419066	10.61	10.60	0.79980
UM0119662	Calmidazolium chloride	10.63	10.56	0.97472
UM0121517	MYCOPHENOLIC ACID	10.68	10.44	0.19783
UM0119979	2-methoxyestradiol	10.69	11.45	0.00167
UM0121249	AMINACRINE	10.71	10.76	0.92425
UM0135484	Temsirolimus (CCI-779)	10.71	13.29	0.07669
UM0121111	alpha-MANGOSTIN	10.75	10.92	0.44556
UM0118623	Cyclosporin A	10.83	10.64	0.65696
UM0119621	Benzotropine mesylate	10.86	12.10	0.03345
UM0118693	Terconazole	10.86	11.41	0.01714
UM0121477	HYDROXYZINE PAMOATE	10.87	12.18	0.17559
UM0119688	Cantharidic Acid	10.95	10.82	0.63414
UM0127891	MK2a Inhibitor	11.03	11.30	0.82170
UM0120732	UM0120732 from UdeM	11.04	11.68	0.02951
UM0129939	UNC0646	11.11	10.63	0.22499
UM0118638	Carbetapentane citrate	11.12	11.96	0.14673
UM0120219	DL-Stearoylcarnitine chloride	11.13	12.69	0.01310
UM0118582	CLEMASTINE	11.20	11.90	0.05546
UM0119800	Eliprodil	11.21	13.05	0.07851
UM0120130	SU 6656	11.26	11.23	0.84917
UM0125807	UM0125807 from UdeM	11.27	11.70	0.42672
UM0119968	L-687,384 hydrochloride	11.29	12.32	0.05344
UM0135506	Arsenic trioxide (Trisenox, As2O3)	11.29	11.29	0.68822
UM0127955	Mubritinib	11.37	7.63	0.06116
UM0121035	7-OXOCHOLESTEROL	11.38	10.36	0.64829
UM0118731	Pentamidine isethionate FGF/VEGF Receptor Tyrosine Kinase Inhibitor	11.40	11.66	0.20927
UM0131000	(PD173074)	11.42	11.59	0.15893
UM0119334	PATULIN	11.43	11.61	0.45909
UM0120205	SKF 96365	11.52	12.49	0.00248
UM0118805	Azacytidine-5	11.59	10.90	0.00685
UM0120639	HOMIDIUM BROMIDE	11.59	12.00	0.82173
UM0119088	Piperacetazine	11.68	12.15	0.13181
UM0135495	MK-2206, AKT inhibitor	11.72	12.19	0.62886
UM0118995	S(-)Eticlopride hydrochloride	11.75	12.98	0.03622
UM0133724	5FU	11.76	11.59	0.13869
UM0127950	Sorafenib (Nexavar)	11.88	10.57	0.02951

UM0135581	UNC1999	11.92	11.24	0.02065
UM0119682	7-Chloro-4-hydroxy-2-phenyl-1,8-	11.93	10.75	0.63765
UM0135578	GSK126	11.96	11.91	0.65696
UM0118177	Proadifen hydrochloride (SKF 525A	11.98	13.14	0.10646
UM0119143	ARTESUNATE	11.98	12.41	0.22104
UM0120832	CHOLEST-5-EN-3-ONE	12.01	13.03	0.01643
UM0119467	CHARTREUSIN	12.05	12.11	0.87201
UM0126615	UM0126615 from UdeM	12.07	12.03	0.40833
UM0135501	SB590885	12.07	11.73	0.07109
UM0125633	UM0125633 from UdeM	12.09	12.09	0.58951
UM0118357	N6-methyladenosine	12.09	13.19	0.25414
UM0125695	UM0125695 from UdeM	12.18	12.86	0.18646
UM0118604	Amiodarone hydrochloride	12.19	12.70	0.03936
UM0135510	Thioridazine hydrochloride	12.35	12.75	0.02475
UM0120016	L-745,870 hydrochloride	12.36	13.29	0.11843
UM0119258	DIACETYLKORSEVERILINE	12.42	13.29	0.11843
UM0096705	UM0096705 from UdeM	12.47	12.83	0.14673
UM0121415	FLUMETHAZONE PIVALATE	12.54	11.57	0.25868
UM0135497	ABT-199	12.63	8.24	0.00311
UM0120474	UM0120474 from UdeM	12.66	12.54	0.68687
UM0022485	UM0022485 from UdeM	12.67	12.97	0.10523
UM0135680	Statine BMS 644950	12.69	11.98	0.51121
UM0118868	Pramoxine hydrochloride	12.70	13.29	0.04064
UM0119908	NSC 95397	12.76	11.87	0.23153
UM0119195	LAPACHONE, beta-	12.79	11.56	0.10330
UM0098937	SPECS_AH-487/40669985	12.90	13.17	0.09585
UM0120206	Salmeterol xinafoate	12.91	13.13	0.36162
UM0119612	Bay 11-7085	12.98	12.96	0.62696
UM0092376	SPECS_AE-848/11419104	13.01	13.03	0.83963
UM0127866	GTP-14564	13.01	13.29	0.14773
UM0118223	Simvastatin	13.01	11.96	0.43777
UM0093450	SPECS_AF-399/40684392	13.02	13.29	0.40293
UM0093794	SPECS_AG-205/07907018	13.04	13.29	0.01396
UM0131006	Flt3 Inhibitor IV	13.12	11.28	0.00467
UM0095749	SPECS_AG-650/41069260	13.12	12.60	0.19084
UM0121469	HYDROXYPROGESTERONE CAPROATE	13.12	12.47	0.84548
UM0126248	UM0126248 from UdeM	13.13	13.00	1.00000
UM0120299	YC-1	13.13	8.67	0.00312
UM0131002	PDGFR Tyrosine Kinase Inhibitor VII	13.15	13.29	0.06319
UM0118216	Dibucaine	13.15	13.29	0.01875
UM0126171	UM0126171 from UdeM	13.15	13.02	0.35132
UM0119434	RUBESCENSIN A	13.16	12.51	0.25028
UM0130968	Selumetinib/AZD6244	13.18	9.93	0.00281
UM0107130	SPECS_AP-906/41650452	13.22	13.29	0.14783
UM0127945	Gefitinib	13.25	13.07	0.26618
UM0093662	SPECS_AF-399/40960315	13.28	13.29	0.11067
UM0121357	ESTRADIOL CYPIONATE	13.29	13.29	0.09021
UM0094890	SPECS_AG-205/36915225	13.29	12.26	0.00497
UM0101838	SPECS_AK-968/37005200	13.29	13.29	0.38102
UM0106805	SPECS_AO-990/15068023	13.29	13.29	0.77422
UM0118273	Flunisolid	13.29	13.29	0.28041
UM0118279	Flumethasone	13.29	13.29	0.27792

UM0118601	Betamethasone	13.29	13.29	0.46718
UM0118717	Budesonide	13.29	13.29	0.74005
UM0118790	Mometasone furoate	13.29	12.67	0.31496
UM0118887	Flurandrenolide	13.29	13.29	0.55721
UM0118891	Halcinonide	13.29	13.29	0.65161
UM0119205	PROSTAGLANDIN E2	13.29	13.29	0.88645
UM0119657	(+)-Chlorpheniramine maleate	13.29	13.29	0.56174
UM0119718	Dihydroergotamine methanesulfonate	13.29	13.29	0.11214
UM0121425	DEXAMETHASONE	13.29	13.29	0.44212
UM0121443	FLUDROCORTISONE ACETATE	13.29	13.29	0.92416
UM0121463	BETAMETHASONE VALERATE	13.29	13.29	0.41784
UM0127952	Imatinib mesylate	13.29	13.29	0.82908
UM0130980	Lenalidomide	13.29	13.29	0.47637
UM0131011	c-Met/RON Dual Kinase Inhibitor	13.29	13.02	0.00773
UM0133752	All-trans retinoic acid (Vesanoid, Tretinoin)	13.29	13.29	0.74784
UM0135490	AZD1208	13.29	12.01	0.75684
UM0092618	SPECS_AE-848/32006058	13.29	13.29	0.02754
UM0093235	SPECS_AF-399/15335038	13.29	13.29	0.50586
UM0093569	UM0093569 from UdeM	13.29	13.29	NA
UM0093796	SPECS_AG-205/07932038	13.29	13.29	0.19397
UM0094058	1,2,2-trimethylpropyl 4-(2-ethoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro-5-	13.29	13.29	0.56047
UM0094107	SPECS_AG-205/12013023	13.29	13.29	0.27084
UM0096165	SPECS_AG-670/41019315	13.29	13.11	0.13820
UM0096176	SPECS_AG-690/08355059	13.29	13.29	0.31752
UM0096781	UM0096781 from UdeM	13.29	13.29	0.13912
UM0097793	SPECS_AG-690/15441703	13.29	13.29	0.94513
UM0098860	SPECS_AH-487/15276024	13.29	13.29	0.19397
UM0099317	UM0099317 from UdeM	13.29	13.29	0.50586
UM0099733	SPECS_AK-777/37037051	13.29	13.29	0.62199
UM0099775	SPECS_AK-778/11708035	13.29	13.29	0.87443
UM0100383	SPECS_AK-968/11841778	13.29	13.04	0.00043
UM0101084	1-(2-bromobenzyl)-4-(3,4,5-trimethoxybenzyl)piperazine	13.29	13.29	0.22669
UM0101184	SPECS_AK-968/15253444	13.29	13.29	0.41723
UM0101480	SPECS_AK-968/15364033	13.29	13.05	0.05709
UM0101845	SPECS_AK-968/37005263	13.29	12.88	0.01150
UM0101847	SPECS_AK-968/37005284	13.29	13.29	0.04612
UM0102603	SPECS_AK-968/41017746	13.29	13.29	0.13912
UM0102657	UM0102657	13.29	13.29	0.02754
UM0102836	SPECS_AK-968/41022109	13.29	13.29	0.56047
UM0103032	UM0103032 from UdeM	13.29	13.29	0.13138
UM0103728	SPECS_AM-807/14959586	13.29	13.29	0.68822
UM0104715	SPECS_AN-648/40682639	13.29	13.29	0.13912
UM0104768	SPECS_AN-648/40925375	13.29	13.29	0.18654
UM0105063	SPECS_AN-698/40705204	13.29	13.29	0.07049
UM0105101	SPECS_AN-698/40745478	13.29	13.29	0.56174
UM0105621	N-[4-(1,3-benzoxazol-2-yl)phenyl]cyclopropanecarboxamide	13.29	13.29	0.38255
UM0105815	SPECS_AN-988/40875350	13.29	13.29	0.19397
UM0106743	UM0106743 from UdeM	13.29	13.29	NA

UM0106825	UM0106825 from UdeM	13.29	13.29	0.22280
UM0107165	UM0107165 from UdeM	13.29	13.29	NA
UM0118129	Cloperastine hydrochloride	13.29	13.29	0.03092
UM0118172	Sulfamethoxy pyridazine	13.29	13.29	NA
UM0118313	Hydrocortisone base	13.29	13.29	0.74239
UM0118901	Atovaquone	13.29	13.29	NA
UM0119063	Methacycline hydrochloride	13.29	13.29	NA
UM0119104	Ribavirin	13.29	13.29	0.16869
UM0119268	GENISTIN	13.29	13.29	NA
UM0119648	Cyclophosphamide	13.29	13.29	NA
UM0119703	2',3'-didehydro-3'-deoxythymidine	13.29	13.29	0.02754
UM0119883	hydroxyurea	13.29	13.29	NA
UM0119978	hydrochloride	13.29	13.29	NA
UM0120224	SU 4312	13.29	13.29	0.73772
UM0120269	Suramin hexasodium	13.29	13.29	NA
UM0120298	WAY-100635 maleate	13.29	13.29	0.56174
UM0120317	(+)-trans-(1R,2R)-U-50488 hydrochloride	13.29	13.29	0.01057
UM0120482	6alpha-METHYLPREDNISOLONE ACETATE	13.29	13.29	0.96204
UM0120587	methylmethane sulfonate	13.29	13.29	NA
UM0120625	FORMESTANE	13.29	13.29	0.19397
UM0120854	LANOSTEROL	13.29	13.29	0.56174
UM0121120	COSMOSIIN HEXAACETATE: apigetrin	13.29	13.29	NA
UM0121301	EZETIMIBE	13.29	13.29	NA
UM0121509	E-64-C	13.29	13.29	NA
UM0123617	UM0123617 from UdeM	13.29	13.29	0.66873
UM0125748	UM0125748 from UdeM	13.29	13.29	0.38255
UM0127622	UM0127622 from UdeM	13.29	13.29	0.56174
UM0129937	EPZ6438	13.29	13.29	0.08661
UM0131110	from UdeM	13.29	13.29	NA
UM0134798	Prednisolone	13.29	13.29	NA
UM0135482	EPZ5676	13.29	13.29	NA
UM0135485	Tipifarnib	13.29	13.29	NA
UM0135488	Vismodegib (RO5450815)	13.29	13.29	0.38255
UM0135505	CPI-613	13.29	13.29	NA
UM0135509	Temozolomide	13.29	13.29	0.50586
UM0135579	UNC2400	13.29	13.29	0.83785

**TABLE S8**

Group	BCLQ ID	Karyotype	TP53	age	sex	Status at sampling	FAB	WBC (x 10 <sup>9</sup> /L)	Tissue	Blast %
CK	03H094	Complex	Altered	56	M	Relapse	AML-M1	85.4	Blood	90
NK	04H112	Normal Karyotype	WT	64	F	Diagnosis	AML-M1	361.2	Bone marrow	91
CK	05H180	Complex	WT	70	M	Diagnosis	AML-M2	200.8	Blood	35
CK	06H004	Complex	Altered	59	F	Diagnosis	Not classifiable by FAB criteria	321	Bone marrow	44
NK	06H133	Normal Karyotype	WT	45	F	Diagnosis	AML-M0	11.9	Blood	60
CK	07H038	Complex	WT	66	M	Diagnosis	AML-M0	9.2	Blood	90
NK	07H134	Normal Karyotype	WT	64	M	Diagnosis	AML-M5	53.1	Blood	81
CK	07H156	Complex	Altered	62	M	Diagnosis	AML-M2	49	Bone marrow	44
NK	08H104	Normal Karyotype	WT	65	M	Diagnosis	AML-M5B	49.3	Bone marrow	60
NK	09H008	Normal Karyotype	WT	67	M	Diagnosis	AML-M5A	65.4	Blood	58
CK	09H084	Complex	Altered	68	F	Diagnosis	Not classifiable by FAB criteria	48.7	Bone marrow	40
NK	09H111	Normal Karyotype	WT	59	F	Diagnosis	AML-M5B	46.8	Blood	80
CK	10H014	Complex	Altered	77	M	Diagnosis	AML-M0	1.3	Bone marrow	72
NK	10H095	Normal Karyotype	WT	65	F	Diagnosis	AML-M1	52	Blood	91
NK	10H101	Normal Karyotype	WT	49	F	Diagnosis	AML-M2	24.5	Bone marrow	70
NK	10H115	Normal Karyotype	WT	43	M	Diagnosis	AML-M1	21.6	Bone marrow	88
NK	10H166	Normal Karyotype	WT	63	M	Diagnosis	Not classifiable by FAB criteria	226.2	Blood	89
CK	10H174	Complex	WT	59	F	Diagnosis	AML-M4	112.7	Bone marrow	70
CK	11H002	Complex	Altered	65	M	post-treatment	AML-M0	18.1	Bone marrow	80
CK	11H017	Complex	WT	35	M	Diagnosis	Not classifiable by FAB criteria	20.3	Bone marrow	56
NK	11H151	Normal Karyotype	WT	61	M	Diagnosis	AML-M1	53.3	Blood	78
CK	11H170	Complex	WT	51	F	Diagnosis	AML-M0	50.5	Blood	94
NK	12H007	Normal Karyotype	WT	27	F	Diagnosis	Not classifiable by FAB criteria	67.2	Blood	71
NK	12H056	Normal Karyotype	WT	62	M	Diagnosis	AML-M1	48.7	Bone marrow	89
NK	12H124	Normal Karyotype	WT	56	F	Diagnosis	AML-M4	49.6	Bone marrow	85
NK	12H171	Normal Karyotype	WT	67	F	Diagnosis	AML-M1	86.7	Bone marrow	95
NK	13H073	Normal Karyotype	WT	87	F	Diagnosis	AML-M1	357	Blood	97
NK	14H007	Normal Karyotype	WT	53	F	Diagnosis	AML-M2	85.7	Blood	80
NK	14H019	Normal Karyotype	WT	42	M	Diagnosis	AML-M0	19.5	Blood	96

**TABLE S9**

Compound name	CK (log <sub>2</sub> (median IC <sub>50</sub> ))	NK (log <sub>2</sub> (median IC <sub>50</sub> ))	p.value
Volasertib (BI6727)	2.14	3.12	0.03200
GSK461363	1.38	2.55	0.00410
Barasertib (AZD1152)	3.79	3.62	0.24880



**TABLE S10**

ANLN	EXO1	RACGAP1
ASF1B	FANCI	RAD51
ASPM	FEN1	RAD51AP1
AURKA	FOXM1	RAD54L
AURKB	GINS2	RECQL4
BIRC5	GTSE1	RNASEH2A
BRCA1	HJURP	RRM1
BUB1	HMMR	RRM2
BUB1B	IQGAP3	SGOL1
C16orf59	KIAA0101	SKA1
CASC5	KIF11	SKA3
CCNA2	KIF14	SPAG5
CCNB1	KIF15	SPC24
CCNB2	KIF18B	SPC25
CCNF	KIF20A	TCF19
CDC20	KIF23	TICRR
CDC25A	KIF24	TIMELESS
CDC25C	KIF2C	TK1
CDC45	KIF4A	TOP2A
CDC6	KIFC1	TPX2
CDCA2	MAD2L1	TRIP13
CDCA3	MCM10	TROAP
CDCA5	MCM4	TTK
CDCA8	MCM6	TYMS
CDK1	MELK	UBE2C
CDKN3	MKI67	UBE2T
CENPA	MND1	WDR76
CENPE	MYBL2	ZWINT
CENPF	NCAPG	
CENPM	NCAPG2	
CEP55	NCAPH	
CHAF1B	NDC80	
CIT	NEK2	
CKAP2L	NUF2	
CKS1B	NUSAP1	
CLSPN	ORC1	
DEPDC1	PCNA	
DEPDC1B	PCNA-AS1	
DIAPH3	PIF1	
DLGAP5	PKMYT1	
DTL	PLK1	
DTYMK	POC1A	
E2F8	POLA1	
ESCO2	POLD1	
ESPL1	POLQ	

**TABLE S11**

PROBE	DESCRIPTION	RANK IN GENE LIST	RANK METRIC SCORE	RUNNING ES	CORE ENRICHMENT
RAD23B	chr9:110045517	14	0.498664409	0.012954669	Yes
RAD21	chr8:117858173	18	0.479830801	0.025850078	Yes
STIL	chr1:47715811	48	0.443641663	0.036695898	Yes
DR1	chr1:93811478	49	0.443492472	0.048728585	Yes
FBXO5	chr6:153291658	79	0.424367726	0.05905147	Yes
NUP50	chr22:45559726	83	0.420635849	0.07034082	Yes
E2F2	chr1:23832920	104	0.409410626	0.08062749	Yes
CHEK1	chr11:125495031	152	0.388893962	0.089248724	Yes
SETD8	chr12:123868704	167	0.381161183	0.09901533	Yes
HIRA	chr22:19318224	168	0.381023586	0.10935314	Yes
BARD1	chr2:215590370	191	0.374302119	0.11860512	Yes
SQLE	chr8:126010720	232	0.360137165	0.1267336	Yes
MKI67	chr10:129894925	309	0.343486249	0.13293193	Yes
TOP1	chr20:39657462	314	0.342222214	0.14205272	Yes
DBF4	chr7:87505693	324	0.33934629	0.15089016	Yes
TFDP1	chr13:114239003	343	0.335899621	0.15926449	Yes
KIF2C	chr1:45205490	346	0.335070521	0.16827337	Yes
LBR	chr1:225589204	366	0.331246972	0.1764804	Yes
KIF23	chr15:69706585	396	0.326290995	0.18414229	Yes
PLK4	chr4:128802016	415	0.323393017	0.1921773	Yes
CCNA2	chr4:122737603	419	0.323093683	0.20082016	Yes
WRN	chr8:30891232	423	0.322300851	0.20944153	Yes
KATNA1	chr6:149916011	499	0.313977003	0.21488029	Yes
NEK2	chr1:211831599	542	0.309326619	0.22154807	Yes
MAPK14	chr6:35995454	544	0.309231073	0.22989695	Yes
POLE	chr12:133200348	558	0.307950228	0.23771828	Yes
CDC25A	chr3:48198668	583	0.305311233	0.2450163	Yes
BIRC5	chr17:76210277	590	0.304401547	0.25302884	Yes
CDC27	chr17:45195311	674	0.296338588	0.2576605	Yes
CDKN3	chr14:54863673	682	0.295534104	0.26539138	Yes
CKS2	chr9:91926113	696	0.293662608	0.27282506	Yes
CCNB2	chr15:59397284	742	0.289079279	0.2788203	Yes
TPX2	chr20:30326904	766	0.287394881	0.28567326	Yes
CENPA	chr2:27008882	788	0.285797715	0.29256505	Yes
AURKA	chr20:54944445	789	0.285796136	0.30031916	Yes
BUB1	chr2:111395275	865	0.280883998	0.3048601	Yes
CDC20	chr1:43824626	867	0.280614138	0.31243253	Yes
CDK1	chr10:62538089	873	0.280081183	0.31982628	Yes
KIF4A	chrX:69509879	976	0.273531944	0.3230589	Yes
TTK	chr6:80714322	1020	0.271434128	0.32865754	Yes
KIF11	chr10:94352825	1050	0.270096391	0.33479476	Yes
ZAK	chr2:173940565	1064	0.269180477	0.34156424	Yes
GSPT1	chr16:11961985	1118	0.26517722	0.3465824	Yes
SLC7A1	chr13:30083551	1126	0.264889151	0.35348186	Yes
PRC1	chr15:91509268	1135	0.264270544	0.36032343	Yes

RACGAP1	chr12:50382945	1139	0.264040738	0.36736408	Yes
EXO1	chr1:242011493	1142	0.2638053	0.37443942	Yes
CUL3	chr2:225334867	1167	0.262283355	0.38057002	Yes
HNRNPD	chr4:83274467	1235	0.258606881	0.38483503	Yes
ATF5	chr19:50431959	1243	0.258177578	0.39155236	Yes
CENPE	chr4:104026963	1299	0.255135506	0.39621598	Yes
TROAP	chr12:49716971	1308	0.254667819	0.402797	Yes
MCM6	chr2:136597196	1351	0.252721697	0.40792897	Yes
CENPF	chr1:214776532	1376	0.251567692	0.41376886	Yes
MYBL2	chr20:42295659	1409	0.25008598	0.41924	Yes
CCNF	chr16:2479395	1418	0.249564424	0.42568254	Yes
KIF20B	chr10:91461347	1423	0.249383241	0.43228447	Yes
CDC7	chr1:91966404	1425	0.249317631	0.43900782	Yes
NDC80	chr18:2571510	1426	0.249310628	0.44577202	Yes
CUL4A	chr13:113863030	1461	0.247442901	0.45108932	Yes
ESPL1	chr12:53662083	1521	0.244142041	0.45529038	Yes
ORC6	chr16:46723558	1524	0.243713483	0.4618206	Yes
SMC2	chr9:106856541	1587	0.240492821	0.46579948	Yes
H2AFX	chr11:118964585	1640	0.237878308	0.47011808	Yes
RAD54L	chr1:46713367	1650	0.237305582	0.476187	Yes
POLQ	chr3:121150273	1767	0.231223226	0.47769678	Yes
CDC6	chr17:38444146	1867	0.226670891	0.4797812	Yes
KIF22	chr16:29802034	1899	0.225293159	0.48462072	Yes
ODC1	chr2:10580497	2013	0.221679926	0.48599482	Yes
HMG2	chr1:26798902	2053	0.22008726	0.49036455	Yes
TOP2A	chr17:38544773	2057	0.219919592	0.49620816	Yes
PLK1	chr16:23690201	2172	0.214143947	0.4973367	Yes
DKC1	chrX:153991017	2214	0.212507397	0.50141865	Yes
CKS1B	chr1:154947118	2216	0.212373599	0.5071396	Yes
TRA2B	chr3:185632358	2326	0.207913116	0.5083045	Yes
PDS5B	chr13:33160564	2387	0.205340207	0.5114117	Yes
KIF5B	chr10:32297938	2428	0.203552991	0.5152918	Yes
ILF3	chr19:10764937	2441	0.203156367	0.520311	Yes
CDC25B	chr20:3767419	2551	0.198451221	0.52121913	Yes
CDC45	chr22:19467349	2578	0.197342977	0.52550566	Yes
SLC38A1	chr12:46576840	2622	0.195635453	0.5290477	Yes
PBK	chr8:27667138	2685	0.193377331	0.53174824	Yes
SYNCRIP	chr6:86317502	2741	0.191380873	0.5346821	Yes
BRCA2	chr13:32889617	2798	0.18952626	0.5375246	Yes
MAD2L1	chr4:120980579	2861	0.187314346	0.54006064	Yes
NUSAP1	chr15:41624892	2974	0.183655664	0.5404441	Yes
KIF15	chr3:44803209	2986	0.183409512	0.5449686	Yes
MCM2	chr3:127317200	3045	0.181034341	0.5474985	Yes
CASC5	chr15:40886447	3070	0.180507243	0.5514104	Yes
CUL5	chr11:107879408	3107	0.179295763	0.5547966	Yes
KPNA2	chr17:66031848	3153	0.177847579	0.55777395	Yes
UBE2C	chr20:44441215	3176	0.177110896	0.5616758	Yes
NUP98	chr11:3696240	3188	0.176802963	0.566021	Yes

H2AFZ	chr4:100869244	3205	0.17616348	0.5701436	Yes
MTF2	chr1:93544792	3271	0.174410343	0.5722063	Yes
SUV39H1	chrX:48553945	3276	0.174304619	0.5767712	Yes
E2F4	chr16:67226068	3388	0.171299458	0.57686055	Yes
TACC3	chr4:1723217	3473	0.169111222	0.57799923	Yes
DDX39A	chr19:14519610	3479	0.168821752	0.58237433	Yes
EWSR1	chr22:29663998	3485	0.168574378	0.5867427	Yes
MCM5	chr22:35796116	3545	0.167061046	0.58885247	Yes
TMPO	chr12:98909676	3558	0.166569158	0.59287894	Yes
WHSC1	chr4:1873123	3570	0.166112527	0.59693414	Yes
CDK4	chr12:58142027	3599	0.16525273	0.6002679	Yes
RBL1	chr20:35624755	3677	0.163072437	0.6015302	Yes
CDKN2C	chr1:51434367	3783	0.159927189	0.6015574	Yes
SLC7A5	chr16:87863629	3913	0.156300202	0.6005005	Yes
CHAF1A	chr19:4402660	4006	0.153998673	0.6009007	Yes
CASP8AP2	chr6:90539619	4228	0.148199841	0.595846	Yes
HMMR	chr5:162887517	4273	0.147401974	0.5980383	Yes
HIST1H2BK	chr6:27106072	4449	0.142634347	0.5947217	Yes
UPF1	chr19:18942744	4478	0.14210926	0.5974275	Yes
TNPO2	chr19:12810008	4496	0.141786501	0.6005763	Yes
HMGB3	chrX:150151763	4508	0.141585618	0.603966	Yes
STAG1	chr3:136055999	4553	0.14038831	0.60596806	Yes
BUB3	chr10:124913760	4617	0.138524532	0.6071393	Yes
PTTG1	chr5:159848814	4672	0.137189448	0.6086439	Yes
MARCKS	chr6:114178527	4790	0.134742692	0.60749495	Yes
SMAD3	chr15:67358195	4885	0.132680312	0.6072346	Yes
MCM3	chr6:52128812	4898	0.132283792	0.6103309	Yes
INCENP	chr11:61891445	4966	0.130851448	0.6111297	Yes
PRIM2	chr6:57179603	5148	0.127234727	0.6071488	Yes
MYC	chr8:128748315	5201	0.126225367	0.6084381	Yes
HN1	chr17:73131338	5205	0.126162171	0.61173785	Yes
PML	chr15:74287014	5278	0.124809682	0.6121674	Yes
NCL	chr2:232319459	5613	0.11939837	0.6016908	No
NASP	chr1:46049660	5712	0.117569014	0.6008562	No
DTYMK	chr2:242615157	6040	0.112107359	0.59046924	No
SRSF2	chr17:74730197	6041	0.112075992	0.59351003	No
YTHDC1	chr4:69176105	6080	0.11133749	0.5949703	No
CDKN1B	chr12:12870204	6197	0.109009065	0.5931642	No
EZH2	chr7:148504464	6540	0.102793604	0.5819086	No
CCNT1	chr12:49082241	6638	0.101110324	0.58066845	No
PAPD7	chr5:6714718	6649	0.100924641	0.5829961	No
SNRPD1	chr18:19192260	6657	0.100793317	0.5854433	No
SFPQ	chr1:35649201	6723	0.099491604	0.58547336	No
PRPF4B	chr6:4021569	7176	0.091467932	0.56939316	No
RPA2	chr1:28218036	7381	0.088434733	0.5634151	No
EGF	chr4:110834040	7387	0.088270143	0.5656047	No
HMGA1	chr6:34204577	7398	0.08809714	0.5675842	No
GIN52	chr16:85711280	7732	0.081555344	0.55612195	No

SRSF1	chr17:56078280	7744	0.081353232	0.5578775	No
STMN1	chr1:26210677	7970	0.0775567	0.55074185	No
ATRX	chrX:76760356	8063	0.076207526	0.54903144	No
H2AFV	chr7:44866488	8121	0.075085022	0.5487278	No
ARID4A	chr14:58765222	8143	0.074826799	0.54989564	No
UBE2S	chr19:55912650	8379	0.071411207	0.54218256	No
FOXN3	chr14:89622516	8402	0.071088009	0.5432079	No
HIF1A	chr14:62162119	8417	0.070707604	0.5445514	No
SRSF10	chr1:24292937	8499	0.069401518	0.543108	No
MEIS2	chr15:37183222	8597	0.06757459	0.540958	No
CUL1	chr7:148395933	8611	0.067247808	0.54224867	No
SMC1A	chrX:53401070	8642	0.066527873	0.5428217	No
AMD1	chr6:111135824	8747	0.065069258	0.5403163	No
NOLC1	chr10:103911933	9105	0.059199091	0.52726185	No
TGFB1	chr19:41836436	9256	0.056476615	0.52263427	No
ODF2	chr9:131217434	9635	0.049867582	0.5084643	No
XPO1	chr2:61705069	9852	0.046208397	0.5008477	No
E2F1	chr20:32263292	10318	0.038610935	0.48279956	No
FANCC	chr9:97861336	10392	0.037458491	0.48081803	No
HSPA8	chr11:122928200	10843	0.030803295	0.46317405	No
DMD	chrX:31137345	11222	0.024699189	0.4483212	No
AURKB	chr17:8108049	11463	0.020244537	0.4390146	No
SMC4	chr3:160117321	11525	0.019166417	0.4370296	No
HNRNPU	chr1:245013602	11829	0.013797833	0.42496094	No
HOXC10	chr12:54378946	11852	0.013349764	0.42441967	No
CTCF	chr16:67596310	13102	-0.003928198	0.37323472	No
TLE3	chr15:70340130	13389	-0.008595753	0.36172307	No
POLA2	chr11:65029432	13795	-0.0154952	0.3455117	No
ORC5	chr7:103766788	13801	-0.015582496	0.34572914	No
TRAI	chr3:49866028	13818	-0.015806632	0.34550095	No
CCND1	chr11:69455873	13863	-0.016523236	0.34414235	No
MNAT1	chr14:61201459	14072	-0.020381425	0.3361536	No
RBM14	chr11:66391685	14359	-0.025582083	0.32510278	No
PURA	chr5:139493708	14746	-0.032205105	0.31012505	No
KPNB1	chr17:45727204	15239	-0.041005403	0.2910331	No
EFNA5	chr5:106712590	15292	-0.041837368	0.29003277	No
SAP30	chr4:174292093	15621	-0.047528826	0.27785262	No
PAFAH1B1	chr17:2496923	16821	-0.066044733	0.2304063	No
BCL3	chr19:45251978	17177	-0.071992353	0.21778113	No
PTTG3P	chr8:67679632	17495	-0.077517919	0.20686637	No
E2F3	chr6:20402137	17710	-0.081362672	0.20028573	No
MT2A	chr16:56642478	17984	-0.086962804	0.19143413	No
CHMP1A	chr16:89710839	18108	-0.08910007	0.18880044	No
PRMT5	chr14:23389720	18505	-0.096523166	0.17515711	No
NOTCH2	chr1:120454176	18562	-0.097289257	0.17549703	No
ABL1	chr9:133589268	18982	-0.105707981	0.16115837	No
NUMA1	chr11:71713910	19014	-0.106414609	0.16277254	No
SLC12A2	chr5:127419483	19893	-0.124427326	0.13009244	No

SS18	chr18:23596217	20112	-0.129544497	0.12465479	No
G3BP1	chr5:151151476	20379	-0.135751367	0.11741437	No
CBX1	chr17:46147414	21285	-0.158427626	0.08454798	No
RASAL2	chr1:178063129	21432	-0.162913382	0.082972445	No
UCK2	chr1:165796732	21605	-0.168777943	0.0804883	No
SMARCC1	chr3:47627378	22659	-0.211969376	0.04299681	No
LMNB1	chr5:126112315	22880	-0.222582161	0.040001296	No
LIG3	chr17:33307517	23182	-0.240849718	0.03417506	No
RPS6KA5	chr14:91337167	23187	-0.241462439	0.04056207	No
HUS1	chr7:48002885	23666	-0.280075163	0.028531393	No
MEIS1	chr2:66662532	23713	-0.284913957	0.034372542	No

**TABLE S12**

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val
HALLMARK_G2M_CHECKPOINT	200	0.6121674	1.8908455	0.0289256	0.2105032	0.083
HALLMARK_HEME_METABOLISM	195	0.7044227	1.8302431	0.0208817	0.1563739	0.115
HALLMARK_MITOTIC_SPINDLE	198	0.4485225	1.7669445	0.0206612	0.1771456	0.179
HALLMARK_E2F_TARGETS	199	0.6491922	1.7437571	0.0573123	0.1605085	0.204
HALLMARK_SPERMATOGENESIS	132	0.3715057	1.6124326	0.0264706	0.2963762	0.366
HALLMARK_TGF_BETA_SIGNALING	54	0.4770935	1.5842228	0.0345572	0.2917738	0.399
HALLMARK_MTORC1_SIGNALING	199	0.4408418	1.5679065	0.085595	0.2736438	0.415
HALLMARK_ANDROGEN_RESPONSE	100	0.3668789	1.5359592	0.0461894	0.2824619	0.456
HALLMARK_UV_RESPONSE_UP	154	0.3780139	1.5171224	0.0397196	0.2768447	0.482
HALLMARK_PROTEIN_SECRETION	96	0.4204671	1.5089183	0.0890269	0.2615056	0.494
HALLMARK_ESTROGEN_RESPONSE_LATE	199	0.3167692	1.4279634	0.0422535	0.3399994	0.588
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	111	0.3966712	1.3960732	0.1666667	0.3590883	0.629
HALLMARK_CHOLESTEROL_HOMEOSTASIS	73	0.3746498	1.378727	0.1369565	0.3553841	0.641
HALLMARK_ESTROGEN_RESPONSE_EARLY	200	0.274007	1.2952799	0.0903614	0.4518961	0.714
HALLMARK_KRAS_SIGNALING_UP	199	0.2761497	1.2794061	0.1089385	0.4511978	0.738
HALLMARK_APICAL_JUNCTION	200	0.2935889	1.261466	0.1984334	0.4549179	0.756
HALLMARK_PI3K_AKT_MTOR_SIGNALING	105	0.3094397	1.2539423	0.1865828	0.441902	0.764
HALLMARK_APICAL_SURFACE	44	0.3261834	1.2441347	0.1636364	0.4328205	0.77
HALLMARK_HYPOXIA	198	0.2795842	1.2246623	0.1690821	0.4377699	0.785
HALLMARK_MYOGENESIS	200	0.2844958	1.2199533	0.2022792	0.422154	0.787
HALLMARK_MYC_TARGETS_V1	198	0.4348958	1.200578	0.3440644	0.4267269	0.8
HALLMARK_ANGIOGENESIS	36	0.3418521	1.1762993	0.2599469	0.4448198	0.829
HALLMARK_IL2_STAT5_SIGNALING	199	0.2586088	1.1310636	0.2702079	0.4957219	0.863
HALLMARK_NOTCH_SIGNALING	32	0.3250612	1.118593	0.300216	0.4954515	0.875
HALLMARK_INTERFERON_ALPHA_RESPONSE	93	0.3885633	1.1053783	0.4037267	0.4937779	0.877
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	199	0.2742646	1.0998935	0.3002755	0.483378	0.879
HALLMARK_UV_RESPONSE_DN	144	0.2445228	1.0728748	0.3037037	0.5055693	0.893
HALLMARK_P53_PATHWAY	200	0.2289003	1.0503923	0.3517699	0.5220799	0.91
HALLMARK_BILE_ACID_METABOLISM	112	0.2387155	1.0415002	0.369898	0.5183294	0.912
HALLMARK_COMPLEMENT	196	0.273164	1.0388726	0.3795309	0.505139	0.914
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	47	0.3014832	0.9670534	0.5073375	0.6019142	0.948
HALLMARK_MYC_TARGETS_V2	58	0.3643124	0.9611996	0.513347	0.592642	0.949
HALLMARK_XENOBIOTIC_METABOLISM	199	0.2179418	0.957076	0.5165877	0.5809904	0.95
HALLMARK_DNA_REPAIR	142	0.2806273	0.9268932	0.5174538	0.6171175	0.958
HALLMARK_APOPTOSIS	160	0.2196675	0.9168644	0.5604396	0.6152847	0.958
HALLMARK_KRAS_SIGNALING_DN	195	0.1848015	0.873707	0.662069	0.6759427	0.97
HALLMARK_INFLAMMATORY_RESPONSE	199	0.2390811	0.8639299	0.5920177	0.6741296	0.972
HALLMARK_PANCREAS_BETA_CELLS	38	0.2188565	0.8288609	0.7175793	0.718412	0.979
HALLMARK_INTERFERON_GAMMA_RESPONSE	191	0.2525077	0.8150839	0.6126316	0.7234674	0.981
HALLMARK_GLYCOLYSIS	198	0.2045166	0.7977095	0.6734234	0.735598	0.984
HALLMARK_IL6_JAK_STAT3_SIGNALING	87	0.219329	0.7753686	0.7209821	0.7576115	0.988
HALLMARK_COAGULATION	135	0.191924	0.7752474	0.7931937	0.7397857	0.988
HALLMARK_HEDGEHOG_SIGNALING	35	0.1941572	0.6944626	0.9033149	0.8372076	0.996
HALLMARK_ADIPOGENESIS	196	0.1748055	0.6209213	0.8636364	0.8970113	0.998
HALLMARK_TNFA_SIGNALING_VIA_NFKB	199	0.1508638	0.4476964	0.9561586	0.9697406	0.998

## SUPPLEMENTAL FIGURES

### Figure S1

(A) Survival in CK AML with and without *TP53* alterations. (B) Aberrant splicing resulting from a splice site mutation. Integrative Genomics Viewer (IGV) captions of sample 11H002 (left panel), carrying a T125T synonymous splice-site mutation and sample 09H084 (middle panel), a representative sample with CK without this mutation. Ratios of average counts for the 21 first kmers in intron 4 over average counts for the 21 last kmers of exon 4 (excluding the one including mutated position), showing unique intron retention in sample with T125T mutation (right panel). (C) Genomic and complementary DNA Sanger sequences for cases with discordance in variant allele frequency (VAF) between RNA and DNA. Sample 08H033 cDNA could not successfully be sequenced, but VAF derived from RNA-sequencing was estimated at 100%. *TP53* mutations VAF are detailed in Table S2. (D) *TP53* expression in CK and non-CK AML. (E) *TP53* isoform expression in non-CK AML. p-value derived from Wilcoxon test. p-value calculated using Log-Rank test. Medians are represented by a black line in dot plots.

### Figure S2

(A) Significance of compound activity based on the status of all mutations recurring in at least 3 samples included in the screen. Response of most active compounds in *JAK2* mutated samples (B) and *RAS* altered samples (C). Only 2 samples were characterized by *FLT3* mutations in the main leukemia clone, therefore the impact of this mutation, which is rare in CK AML, could not be assessed.

### Figure S3

(A) Differential analysis of cell cycle genes (GO:0007049) and *MKI67* expression in our AML samples dependent of their tissue provenance: bone marrow (BM) or peripheral blood. (B) *PLK1* and *MKI67* mRNA expression in BM and blood specimens. CK samples are depicted in red, non-CK in grey (upper panel). Within each subgroup of tissue source, *PLK1* and *MKI67* expression is compared between CK and non-CK AML (lower panel). Medians are represented by a black line.

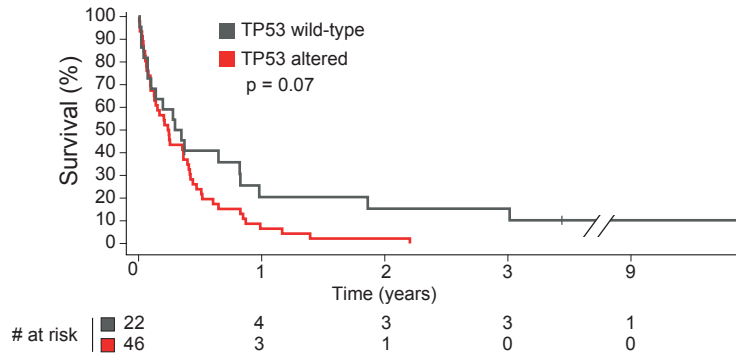
### Figure S4

(A) Mouse weight followed over time in vehicle, cytarabine and volasertib treated mice after transplantation with HL-60 leukemic cells (n=6 for each condition). (B) Mouse weight followed over time in vehicle, cytarabine and volasertib treated mice after transplantation with 09H046 AML cells (n=6 for each condition).

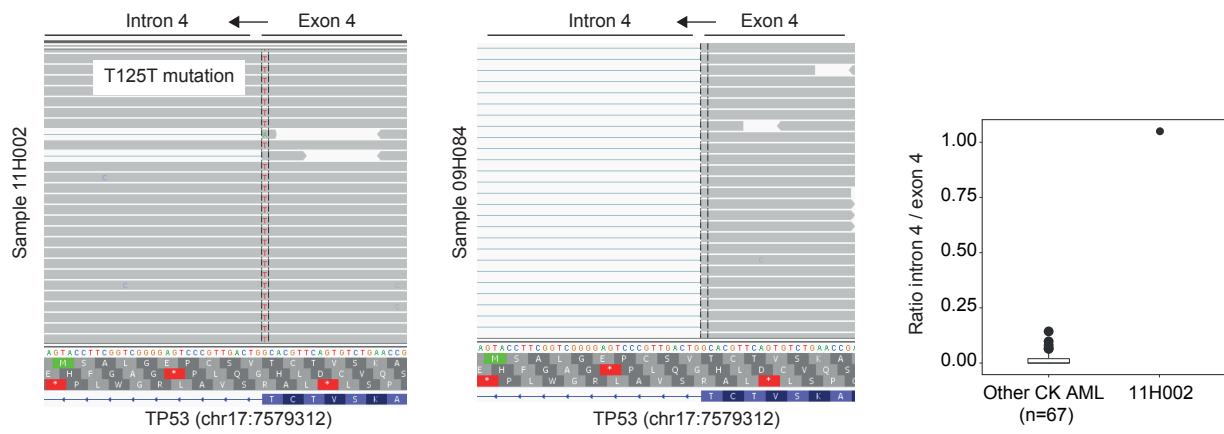


**Figure S1**

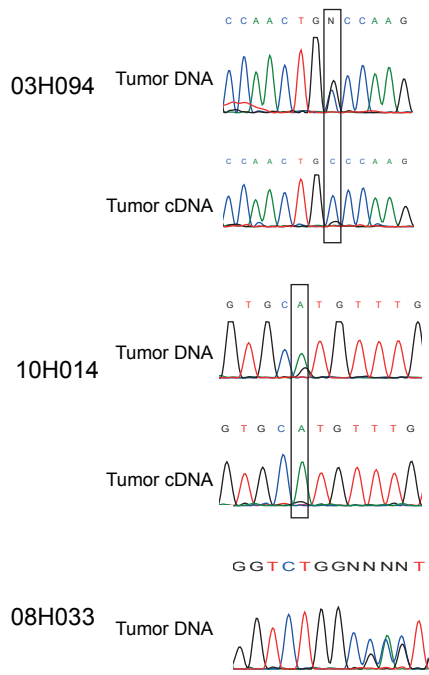
**A**



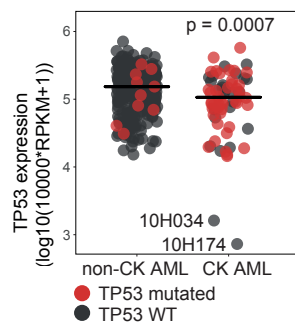
**B**



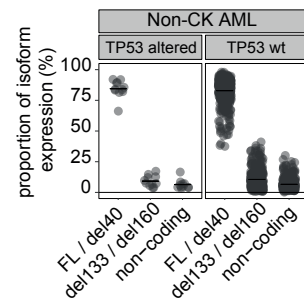
**C**



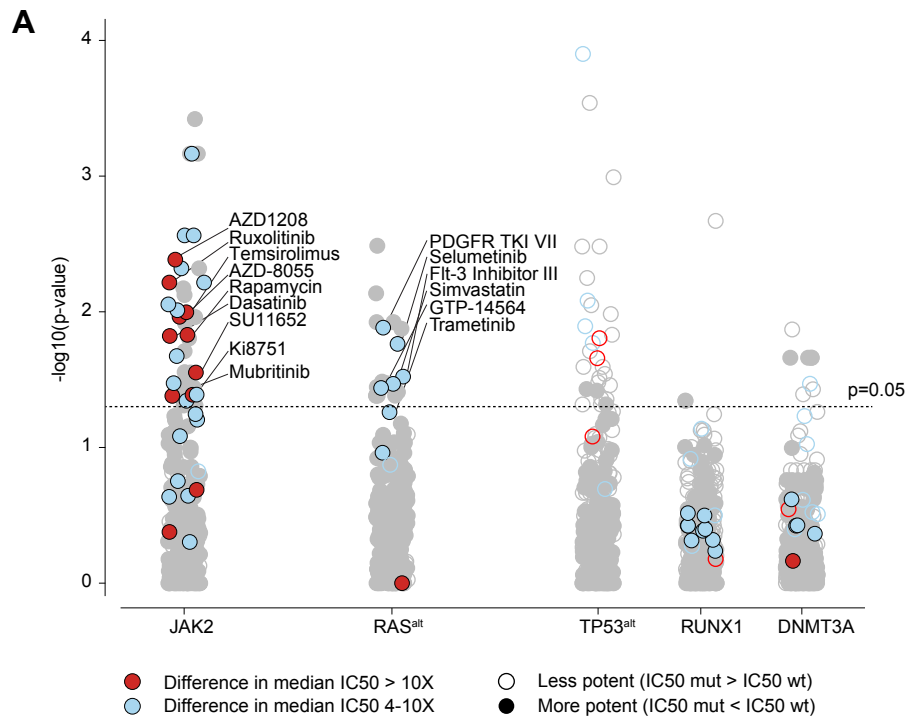
**D**



**E**



**Figure S2**



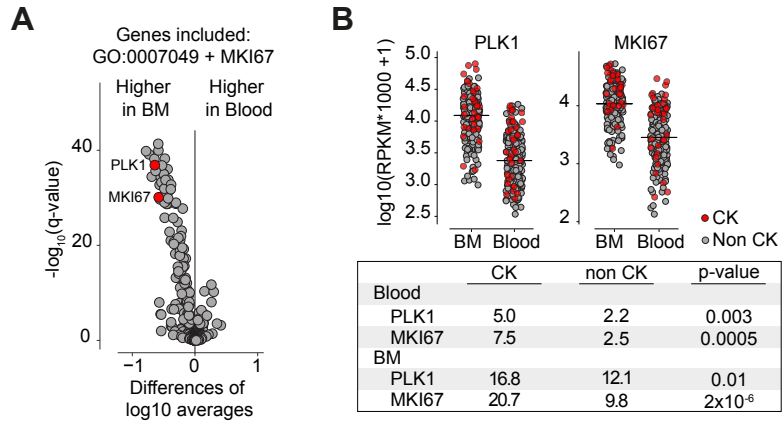
**B**

Compound	Target	p-value	Median IC <sub>50</sub> JAK2 <sup>mut</sup> (nM)	Median IC <sub>50</sub> JAK2 <sup>wt</sup> (nM)
AZD-1208	pim kinase	0.004	150	>10000
Ruxolitinib	JAK1/2	0.006	64	664
Temsirolimus	mTOR	0.010	10	3614
AZD-8055	mTOR	0.011	6	62
Rapamycin	mTOR	0.015	<4	>10000
Dasatinib	tyrosine kinases	0.015	<4	321
SU11652	tyrosine kinases	0.028	10	145
Ki8751	VEGFR2	0.041	130	1705
Mubritinib	Her2	0.042	153	5159

**C**

Compound	Target	p-value	Median IC <sub>50</sub> RAS <sup>alt</sup> (nM)	Median IC <sub>50</sub> RAS <sup>wt</sup> (nM)
PDGFR TKI VII	PDGFR	0.013	2427	>10000
Selumetinib	MEK1	0.017	2117	>10000
Flt-3 inhibitor III	FLT3	0.030	105	424
Simvastatin	HMG-CoA reductase	0.034	1134	9506
GTP-14564	tyrosine kinases	0.036	2021	>10000
Trametinib	MEK1/2	0.055	5	37

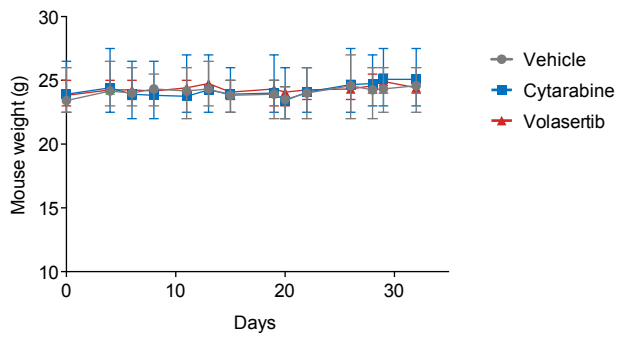
**Figure S3**



**Figure S4**

**A**

**HL-60 cell line:**



**B**

**09H046 primary human AML:**

