Title: *PHF6* and *DNMT3A* Mutations are Enriched in Distinct Subgroups of Mixed Phenotype Acute Leukemia with T-lineage Differentiation

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Supplemental materials

Supplemental Methods

Sequencing Data Generation on sorted blasts

Three tumor samples from patients with Mixed Phenotype Acute Leukemia (MPAL) were sequenced using the Hemepact clinical assay. Short insert paired-end reads were aligned to the GRCh37 reference human genome with 1000 genomes decoy contigs using BWA-mem[1]. After alignment, we obtained an average of 500X coverage per sample.

Somatic Mutation Calling on sorted blasts

Substitutions

Single base substitutions were called using CaVEMan (http://cancerit.github.io/CaVEMan/). As described previously[2], the algorithm compares sequence data from each tumour sample albeit with an unmatched non-cancerous sample and calculates a mutation probability at each genomic locus. To improve specificity, a number of post-processing filters were applied as follows:

1. At least a third of the alleles containing the mutant must have base quality >= 25.
2. If mutant allele coverage >= 10X, there must be a mutant allele of at least base quality 20 in the middle 3rd of a read. If mutant allele coverage is < 10X, a mutant allele of at least base quality 20 in the first 2/3 of a read is acceptable.
3. The mutation position is marked by <3 reads in any sample in the unmatched normal panel.
4. The mutant allele proportion must be >5 times than that in the unmatched normal sample (or it is zero in the unmatched normal).
5. If the mean base quality is <20 then less than 96% of mutations carrying reads are in one direction.
6. Mutations within simple repeats, centromeric repeats, regions of excessive depth (https://genome.ucsc.edu/) and low mapping quality were excluded.

Additional unmatched normal filtering was performed using a set of unmatched normal samples. Mutations that were detected in >5% of the unmatched normal normal panel at >=5% mutant allele burden were excluded.

Variant annotation was done in Ensembl v74 using VAGrENT[3].

Small insertions and deletions: Pindel

Small somatic insertions and deletions (indels) were identified using a modified version of Pindel (https://github.com/cancerit/cgpPindel)[4]. To improve specificity, a number of post-processing filters were applied that required the following:

1) For regions with sequencing depth <200X, mutant variant must be present in at least 8% of total reads.
2) For regions with sequencing depth >=200X, mutant variant must be present in at least 4% of total reads.
3) The region with the variant should have <= 9 small (<4 nucleotides) repeats.
4) The variant is not seen in any reads in the unmatched normal sample or the unmatched normal panel.
5) The number of Pindel calls in the tumor sample is greater than 4 and either:

a. The number of mutant reads mapped by BWA in the tumor sample is greater than 0 or

b. The number of mutant reads mapped by BWA in the tumor sample is equal to 0 but there are no repeats in the variant region and there are reads mapped by Pindel in the tumor sample on both the positive and negative strand.
6) Pindel 'SUM-MS' score (sum of the mapping scores of the reads used as anchors) >=150
Additional unmatched normal filtering was performed using a set of unmatched normal samples (n=221). Mutations that were detected in >1% of the unmatched normal normal panel at >=1% mutant allele burden were excluded.

Variant annotation was done in Ensembl v74 using VAGrENT[3].
For both substitutions and indels, variants that may have failed post processing filtering criteria but mapped to recurrent oncogenic mutations in COSMIC were retained for manual curation.

Secondary pipelines for substitution and indel discovery and post call filters:
To identify subclonal variants at very low frequencies in the tumor samples mutation calling using secondary pipelines were done. Strelka 2 (v2.8.3) [https://doi.org/10.1101/192872] was used to call point mutations and indels using tumor sample and matched normal. All "PASS" calls were examined for their presence in Caveman and Pindel outputs; all other filters from Strelka 2 were ignored. Calls uniquely identified by Strelka2 were retained for downstream analysis.

The following filters were applied on calls identified by primary and secondary pipelines:
Filter calls with > 3% MAF in Exac (Version 0.3) or 1000 Genomes
Filter calls with > 0.5% MAF in Exac or 1000 Genomes unless present in COSMIC (v81) [PMC2705836]
Filter synonymous and intronic (functionally inconsequential) variant

Expression Analysis

The RNA-Seq data set was mapped in the human transcriptome (hg19) using the quasi-mapping approach Salmon (v. 0.10.0) software[5]. The conversion from salmon estimated the relative abundance of this transcript (TPM) to gene level counts was performed using the R package tximport (v. 1.6.0)[6].

To analyse the relationships and differences of expression data across samples, a hierarchical clustering was applied using 98 genes that have been previously shown to be associated with T-cell, B-cell or Myeloid signatures[7] using ComplexHeatmap package of R/Bioconductor, v.1.19.1[8].

References

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4. Raine KM, Hinton J, Butler AP, et al. cgpPindel: Identifying Somatically Acquired Insertion and Deletion Events from Paired End Sequencing. *Curr Protoc Bioinformatics*. 2015;52:15.17.11-12.
5. Patro R, Duggal G, Love MI, Irizarry RA, Kingsford C. Salmon provides fast and bias-aware quantification of transcript expression. *Nat Methods*. 2017;14(4):417-419.
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7. Abbas AR, Baldwin D, Ma Y, et al. Immune response in silico (IRIS): immune-specific genes identified from a compendium of microarray expression data. *Genes Immun*. 2005;6(4):319-331.
8. Gu Z, Eils R, Schlesner M. Complex heatmaps reveal patterns and correlations in multidimensional genomic data. *Bioinformatics*. 2016;32(18):2847-2849.

1.

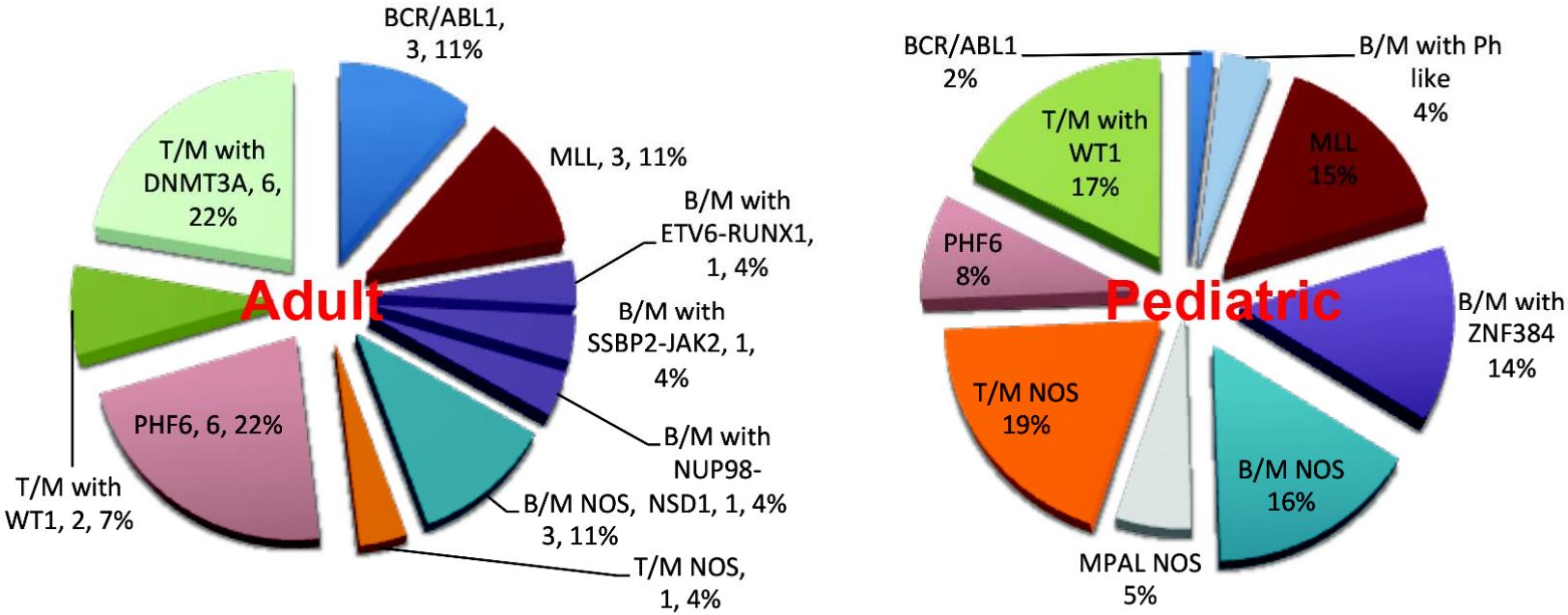

Figure S1 Updated MPAL classification based on genetic aberrations. Differences and similarities of genetic basis are observed between adult (our study) and pediatric MPAL (Alexander et al. Nature 2018). Although many genetic aberrations are shared between adult and pediatric MPAL, DNMT3A mutations are prevalent in adult MPAL but absent in pediatric ones. On the other hand, ZNF384 rearrangements are common in pediatric MPAL but absent in adult ones.

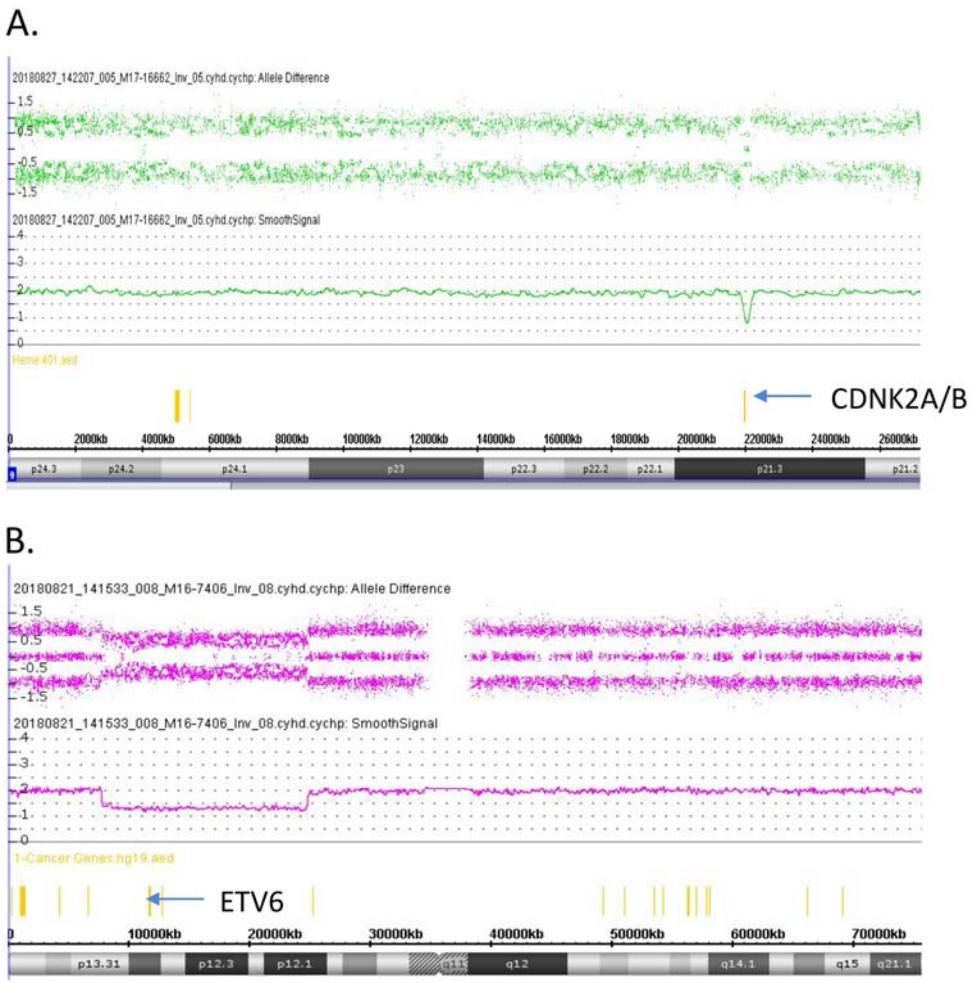

Figure S2 Representative microarray results. Microarray tests detected A). CN-LOH of 9p and a focal deletion of CDKN2A/B (9p21.3, arrow) in case 3, and B). An interstitial deletion of 12p involving the ETV6 gene (12p13.2, arrow) in case 16.

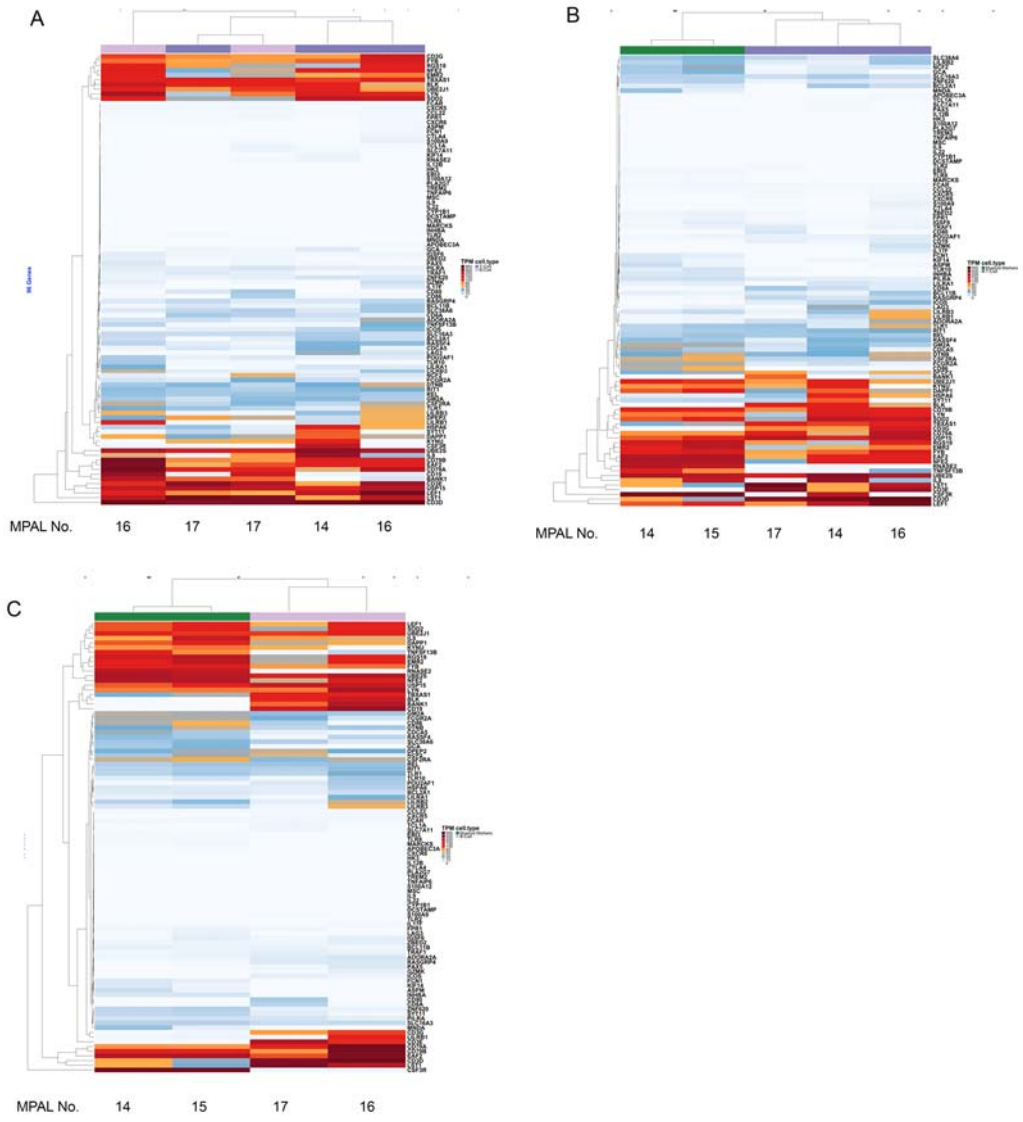
A
MPAL No. 16 17 17 14 16
B
MPAL No. 14 15 17 14 16
C
MPAL No. 14 15 17 16

Figure S3 Differential gene expression in sorted population. A, T-blasts vs B-blasts; B, Myeloid blasts vs T-blasts; C, Myeloid blasts vs B-blasts.

Table S1 Workflow of the sequencing studies performed on MPAL cases

Case	WHO.category	T-lineage (0= No, 1=Yes)	Molecular	Fusion genes	Archer or RAN-seq (1=done)	RainDance (1=done)	Foundation (1=done)	SNP-Array (1=done)
1	MPAL with t(v;11q23)	0	others	*MLL-AF4*	1	1	ND	ND
2	MPAL with t(v;11q23)	0	others	*MLL-AF4*	1	1	1	ND
3	MPAL with t(v;11q23)	0	others	*MLL-AF4*	1	1	1	1
4	MPAL with t(9;22)(q34;q11.2)	0	others	*BCR-ABL1*	1	1	1	ND
5	MPAL with t(9;22)(q34;q11.2)	0	others	*BCR-ABL1*	1	1	ND	1
6	MPAL with t(9;22)(q34;q11.2)	0	others	*BCR-ABL1*	1	1	ND	1
7	MPAL B/Myeloid, NOS	0	others	Negative	**1***	1	ND	1
8	MPAL B/Myeloid, NOS	0	others	*NUP98-NSD1*	**1***	1	ND	1
9	MPAL B/Myeloid, NOS	0	others	*ETV6-RUNX1*	1*	1	1	ND
10	MPAL B/Myeloid, NOS	0	others	*SSBP2-JAK2*	1*	1	1	ND
11	MPAL B/Myeloid, NOS	0	others	Negative	**1***	1	1	1
12	MPAL B/Myeloid, NOS	0	PHF6	Unknown	ND	1	ND	ND
13	MAPL T/Myeloid, NOS	1	PHF6	*PICALM-MLLT10*	1*	1	1	ND
14	MAPL, NOS	1	PHF6	*SEM4B-BCL11A*	1*	1	1	ND

15	MAPL T/Myeloid, NOS	1	PHF6	Negative	**1***	1	ND	ND
16	MPAL, NOS	1	PHF6	*SET-NUP214*	1*	1	1	1
17	MPAL, NOS	1	PHF6	Negative	1*	1	1	ND
18	MAPL T/Myeloid, NOS	1	DNMT3A	Unknown	ND	1	ND	1
19	MAPL T/Myeloid, NOS	1	DNMT3A	Negative	**1***	1	ND	1
20	MAPL T/Myeloid, NOS	1	DNMT3A	Negative	**1***	1	ND	1
21	MAPL T/Myeloid, NOS	1	DNMT3A	Negative	**1***	1	ND	1
22	MAPL T/Myeloid, NOS	1	DNMT3A	*PICALM-MLLT10*	1*	1	1	1
23	MAPL T/Myeloid, NOS	1	DNMT3A	Unknown	ND	1	ND	ND
24	MAPL T/Myeloid, NOS	1	others	Negative	1*	1	ND	ND
25	MAPL T/Myeloid, NOS	1	others	Negative	**1***	1	ND	1
26	MAPL T/Myeloid, NOS	1	others	Negative	**1***	1	ND	1
27	MAPL T/Myeloid, NOS	1	ND	Unknown	ND	ND	ND	ND
28	MPAL with t(v;11q23)	0	ND	Unknown	ND	ND	ND	ND
29	MPAL B/Myeloid, NOS	0	ND	Unknown	ND	ND	ND	ND

* RNA-seq data. ND, not done.

Table S2 Antibody panels of immunophenotyping by flow cytometry

Myeloid tube 1	Myeloid tube 2	Myeloid tube 3	B-ALL	T-ALL	Intracytoplasmics
CD15 FITC (BC)	CD64 FITC (BC)	CD7 BB515 (BD HORIZON)	CD20 FITC (BD)	cyCD3 Alexa-488 (BD)	MPO FITC (BC)
CD33 PE (BC)	CD123 PE (BD PHARM)	CD56 PE (BC)	CD34 PE (BC)	CD7 PE (BD)	cyCD79a PE (BC)
CD117 PC5 (BC)	CD14 PC5 (BC)	CD5 PerCP-Cy5.5 (BD)	CD10 PC5.5 (BC)	CD56 PC5 (BC)	CD19 PC7 (BC)
CD13 PE-Cy7 (BD)	CD13 PE-Cy7 (BD)	CD33 PC7 (BC)	CD33 PC7 (BC)	CD16 PC5 (BC)	CD34 PerCP-Cy5.5 (BD)
CD34 APC (BC)	CD34 APC (BC)	CD34 APC (BC)	CD58 APC (BC)	CD5 PC7 (BC)	cyCD3 APC (BC)
CD71 APC-A700 (BC)	CD16 APC-A700 (BC)	CD4 APC-A700 (BC)	CD45 APC-H7 (BD)	CD3 APC (BD)	CD45 APC-H7 (BD)
CD38 APC-A750 (BC)	CD38 APC-A750 (BC)	CD38 APC-A750 (BC)	CD19 BV421 (BD)	CD10 APC-R700 (BD)	CD3 BV421 (BD HORIZON)
HLA-DR PAC BLUE (BC)	HLA-DR PAC BLUE (BC)	CD2 BV421 (BD PHARM)	CD38 BV510 (BD)	CD38 APC-A750 (BC)	
CD45 V500c (BD)	CD45 V500C (BD)	CD45 V500c (BD)		CD48 BV421 (BD)	
CD19 BV605 (BIOLEGEND)	CD11b BV605 (BD HORIZON)	CD25 BV605 (Biolegend)		CD45 V500c (BD)	

Table S3 Flow cytometric immunophenotype of MPAL

Case	MPO	CD33	CD13	CD15	CD14	CD64	CD11b	CD56	CD123	HLADR	TdT*	CD2	cyCD3	CD4	CD5	CD7	CD8	CD19	cyCD79a	CD20	CD22	CD10	CD34	CD117
1	0	1	0	0	0	1	1	0	1	0	1	0	0	0	0	0	0	1	1	0	0	0	1	0
2	0	1	1	1	0	1	1	0	1	1	1	0	0	0	0	0	0	1	1	0	0	0	1	0
3	1	1	1	1	0	1	1	0	1	1	1	0	0	0	0	0	0	1	1	0	0	0	1	0
4	1	1	1	1	0	0	1	0	1	1	1	0	0	0	0	0	0	1	1	0	ND	1	1	0
5	1	1	1	0	0	0	0	1	1	1	1	0	0	0	0	0	0	1	1	0	0	0	1	0
6	1	1	1	1	0	0	0	0	1	1	1	0	0	0	0	0	0	1	1	0	0	0	1	0
7	0	1	1	0	0	0	0	0	1	1	1	0	0	0	0	1	0	1	1	1	ND	0	1	1
8	1	1	1	1	0	0	0	0	1	1	1	0	0	0	0	0	0	1	1	0	0	0	1	1
9	1	1	1	1	0	0	0	0	1	1	1	0	0	0	0	0	0	1	1	0	ND	1	1	1
10	0	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	1	1	0	ND	1	1	1
11	1	1	1	1	0	1	0	0	1	1	1	1	0	0	0	0	0	1	1	0	ND	1	1	0
12	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	1	1	1	ND	1	1	0
13	1	1	0	1	0	1	1	1	1	0	1	0	1	0	1	1	0	0	1	0	0	0	1	0
14	1	1	0	0	0	0	0	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1
15	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	0	0	1	0	0	0	0	1
16	0	1	0	0	0	0	1	0	1	1	1	1	1	0	1	1	0	1	1	0	ND	0	0	0
17	1	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	0	1	1	1	1	1	0	1
18	0	1	1	0	1	1	1	0	1	1	1	1	1	0	0	1	0	0		0	ND	0	1	1
19	1	1	1	0	0	0	1	0	1	1	1	0	1	0	1	1	0	0	0	0	0	0	1	0
20	1	1	1	1	0	0	1	1	1	1	ND	1	1	0	1	1	0	0	0	0	0	0	1	0
21	1	1	1	1	0	0	1	1	1	1	ND	1	1	0	1	1	0	0	0	0	0	0	1	0
22	1	1	1	1	0	0	0	0	1	1	ND	0	1	0	1	1	0	0	1	0	0	1	1	1
23	1	1	1	0	0	0	0	1	1	1	1	0	1	1	1	1	0	0		0	0	0	1	1
24	1	0	1	1	0	0	1	1	1	1	1	1	1	0	0	1	0	0	0	0	ND	0	1	1
25	1	1	1	0	0	0	0	0	1	1	1	1	1	0	0	1	0	0	0	0	ND	0	1	1
26	1	0	1	0	0	0	0	0	1	1	1	1	1	0	0	1	0	0	0	0	ND	0	1	1
27	1	1	0	0	0	0	0	1	1	1	1	0	1	0	0	1	0	0	0	0	ND	0	1	0
28	1	1	1	0	0	1	1	0	1	1	1	0	0	0	1	1	0	1	1	0	1	0	1	1
29	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	1	1	0	1	1	1	1

* Also included data from immunohistochemical stain. ND, not done.

Table S4 Gene list of RainDance panel

ASXL1	IDH1	MPL	SH2B3
CBL	IDH2	NPM1	SUZ12
CEBPA	JAK1	NRAS	TET1
DNMT3A	JAK2	PHF6	TET2
ETV6	JAK3	PTEN	TP53
EZH2	KIT	RUNX1	TYK2
FLT3	KRAS	SF3B1	WT1

Table S5 Gene list of FoundationOne Heme panel

Gene list--Entire coding sequence (base substitutions, indels, copy number alterations)

ABL1	CBFB	DUSP9	FOXL2	IRF1	MPL	PIM1	SOX10	ZNF217
ACTB	CBL	EBF1	FOXO1	IRF4	MRE11A	PLCG2	SOX2	ZNF24
AKT1	CCND1	ECT2L	FOXO3	IRF8	MSH2	POT1	SPEN	ZNF703
AKT2	CCND2	EED	FOXP1	IRS2	MSH3	PPP2R1A	SPOP	ZRSR2
AKT3	CCND3	EGFR	FRS2	JAK1	MSH6	PRDM1	SRC	
ALK	CCNE1	ELP2	GADD45B	JAK2	MTOR	PRKAR1A	SRSF2	
AMER1	CCT6B	EP300	GATA1	JAK3	MUTYH	PRKDC	STAG2	
APC	CD22	EPHA3	GATA2	JARID2	MYC	PRSS8	STAT3	
APH1A	CD274	EPHA5	GATA3	JUN	MYCL	PTCH1	STAT4	
AR	CD36	EPHA7	GID4	KAT6A	MYCN	PTEN	STAT5A	
ARAF	CD58	EPHB1	GNA11	KDM2B	MYD88	PTPN11	STAT5B	
ARFRP1	CD70	ERBB2	GNA12	KDM4C	MYO18A	PTPN2	STAT6	
ARHGAP26	CD79A	ERBB3	GNA13	KDM5A	NCOR2	PTPN6	STK11	
ARID1A	CD79B	ERBB4	GNAQ	KDM5C	NCSTN	PTPRO	SUFU	
ARID2	CDC73	ERG	GNAS	KDM6A	NF1	RAD21	SUZ12	
ASMTL	CDH1	ESR1	GPR124	KDR	NF2	RAD50	TAF1	
ASXL1	CDK12	ETS1	GRIN2A	KEAP1	NFE2L2	RAD51	TBL1XR1	
ATM	CDK4	ETV6	GSK3B	KIT	NFKBIA	RAF1	TCF3	
ATR	CDK6	EXOSC6	GTSE1	KLHL6	NKX2-1	RARA	TCL1A	
ATRX	CDK8	EZH2	HDAC1	KMT2A	NOD1	RASGEF1A	TET2	
AURKA	CDKN1B	FAF1	HDAC4	KMT2C	NOTCH1	RB1	TGFBR2	
AURKB	CDKN2A	FAM46C	HDAC7	KMT2D	NOTCH2	RELN	TLL2	
AXIN1	CDKN2B	FANCA	HGF	KRAS	NPM1	RET	TMEM30A	
AXL	CDKN2C	FANCC	HIST1H1C	LEF1	NRAS	RHOA	TMSB4XP8	
B2M	CEBPA	FANCD2	HIST1H1D	LRP1B	NT5C2	RICTOR	TNFAIP3	
BAP1	CHD2	FANCE	HIST1H1E	LRRK2	NTRK1	RNF43	TNFRSF11A	
BARD1	CHEK1	FANCF	HIST1H2AC	MAF	NTRK2	ROS1	TNFRSF14	
BCL10	CHEK2	FANCG	HIST1H2AG	MAFB	NTRK3	RPTOR	TNFRSF17	
BCL11B	CIC	FANCL	HIST1H2AL	MAGED1	NUP93	RUNX1	TOP1	
BCL2	CIITA	FAS	HIST1H2AM	MALT1	NUP98	S1PR2	TP53	
BCL2L2	CKS1B	FBXO11	HIST1H2BC	MAP2K1	P2RY8	SDHA	TP63	
BCL6	CPS1	FBXO31	HIST1H2BJ	MAP2K2	PAG1	SDHB	TRAF2	
BCL7A	CREBBP	FBXW7	HIST1H2BK	MAP2K4	PAK3	SDHC	TRAF3	
BCOR	CRKL	FGF10	HIST1H2BO	MAP3K1	PALB2	SDHD	TRAF5	
BCORL1	CRLF2	FGF14	HIST1H3B	MAP3K14	PASK	SERP2	TSC1	
BIRC3	CSF1R	FGF19	HNF1A	MAP3K6	PAX5	SETBP1	TSC2	
BLM	CSF3R	FGF23	HRAS	MAP3K7	PBRM1 PC	SETD2	TSHR	
BRAF	CTCF	FGF3	HSP90AA1	MAPK1	PCBP1	SF3B1	TUSC3	
BRCA1	CTNNA1	FGF4	ICK	MCL1	PCLO	SGK1	TYK2	
BRCA2	CTNNB1	FGF6	ID3	MDM2	PDCD1	SMAD2	U2AF1	
BRD4	CUX1	FGFR1	IDH1	MDM4	PDCD11	SMAD4	U2AF2	

BRIP1	CXCR4	FGFR2	IDH2	MED12	PDCD1LG2	SMARCA1	VHL
BRSK1	DAXX	FGFR3	IGF1R	MEF2B	PDGFRA	SMARCA4	WDR90
BTG2	DDR2	FGFR4	IKBKE IKZF1	MEF2C	PDGFRB	SMARCB1	WHSC1
BTK	DDX3X	FHIT	IKZF2	MEN1	PDK1	SMC1A	WISP3
BTLA	DNM2	FLCN	IKZF3	MET	PHF6	SMC3	WT1
C11orf30	DNMT3A	FLT1	IL7R	MIB1	PIK3CA	SMO	XBP1
CAD	DOT1L	FLT3	INHBA	MITF	PIK3CG	SOCS1	XPO1
CALR	DTX1	FLT4	INPP4B	MKI67	PIK3R1	SOCS2	YY1AP1
CARD11	DUSP2	FLYWCH1	INPP5D	MLH1	PIK3R2	SOCS3	ZMYM3

Selected DNA rearrangements

ALK	**ETV4**	**KMT2A(MLL)**	**TRG**
BCL2	ETV5	MYC	
BCL6	ETV6	NTRK1	
BCR	EWSR1	PDGFRA	
BRAF	FGFR2	PDGFRB	
CCND1	IGH	RAF1	
CRLF2	IGK	RARA	
EGFR	IGL	RET	
EPOR	JAK1	ROS1	
ETV1	JAK2	TMPRSS2	

Seleted RNA gene fusions

ABI1	**CREBBP**	**HMGA1**	**MUC1**	**PTCH1**	**TP63**
ABL1	CRLF2	HMGA2	MYB	PTK7	TPM3
ABL2	CSF1	HOXA11	MYC	RABEP1	TPM4
ACSL6	CTNNB1	HOXA13	MYH11	RAF1	TRIM24
AFF1	DDIT3	HOXA3	MYH9	RALGDS	TRIP11
AFF4	DDX10	HOXA9	NACA	RAP1GDS1	TTL

ALK	DDX6	HOXC11	NBEAP1	RARA	TYK2
ARHGAP26	DEK	HOXC13	NCOA2	RBM15	USP6
ARHGEF12	DUSP22	HOXD11	NDRG1	RET	WHSC1
ARID1A	EGFR	HOXD13	NF1	RHOH	WHSC1L1
ARNT	EIF4A2	HSP90AA1	NF2	RNF213	YPEL5
ASXL1	ELF4	HSP90AB1	NFKB2	ROS1	ZBTB16
ATF1	ELL	IGH	NIN	RPL22	ZMYM2
ATG5	ELN	IGK	NOTCH1	RPN1	ZNF384
ATIC	EML4	IGL	NPM1	RUNX1	ZNF521
BCL10	EP300	IKZF1	NR4A3	RUNX1T1	
BCL11A	EPOR	IL21R	NSD1	RUNX2	
BCL11B	EPS15	IL3	NTRK1	SEC31A	
BCL2	ERBB2	IRF4	NTRK2	SEPT5	
BCL3	ERG	ITK	NTRK3	SEPT6	
BCL6	ETS1	JAK1	NUMA1	SEPT9	
BCL7A	ETV1	JAK2	NUP214	SET	
BCL9	ETV4	JAK3	NUP98	SH3GL1	
BCOR	ETV5	JAZF1	NUTM2A	SLC1A2	
BCR	ETV6	KAT6A	OMD	SNX29	
BIRC3	EWSR1	KDSR	P2RY8	SRSF3	
BRAF	FCGR2B	KIF5B	PAFAH1B2	SS18	
BTG1	FCRL4	KMT2A	PAX3	SSX1	
CAMTA1	FEV	LASP1	PAX5	SSX2	
CARS	FGFR1	LCP1	PAX7	SSX4	
CBFA2T3	FGFR1OP	LMO1	PBX1	STAT6	
CBFB	FGFR2	LMO2	PCM1	STL	
CBL	FGFR3	LPP	PCSK7	SYK	
CCND1	FLI1	LYL1	PDCD1LG2	TAF15	

CCND2	FNBP1	MAF	PDE4DIP	TAL1
CCND3	FOXO1	MAFB	PDGFB	TAL2
CD274	FOXO3	MALT1	PDGFRA	TBL1XR1
CDK6	FOXO4	MDS2	PDGFRB	TCF3
CDX2	FOXP1	MECOM	PER1	TCL1A
CHIC2	FSTL3	MKL1	PHF1	TEC
CHN1	FUS	MLF1	PICALM	TET1
CIC	GAS7	MLLT1	PIM1	TFE3
CIITA	GLI1	MLLT10	PLAG1	TFG
CLP1	GMPS	MLLT3	PML	TFPT
CLTC	GPHN	MLLT4	POU2AF1	TFRC
CLTCL1	HERPUD1	MLLT6	PPP1CB	TLX1
CNTRL	HEY1	MN1	PRDM1	TLX3
COL1A1	HIP1	MNX1	PRDM16	TMPRSS2
CREB3L1	HIST1H4I	MSI2	PRRX1	TNFRSF11A
CREB3L2	HLF	MSN	PSIP1	TOP1

Table S6 Gene list of MSK IMPACT panel

ABL1	BCL11B	CEBPA	ETNK1	HDAC1	JAK1	MLH1	PCBP1	REL	SMG1	U2AF2
ACTG1	BCL2	CHEK1	ETV6	HDAC4	JAK2	MOB3B	PDCD1	RET	SMO	UBR5
AKT1	BCL6	CHEK2	EZH2	HDAC7	JAK3	MPEG1	PDGFRA	RHOA	SOCS1	VAV1
AKT2	BCOR	CIC	FAM46C	HGF	JARID2	MPL	PDGFRB	RICTOR	SOX2	VAV2
AKT3	BCORL1	CIITA	FANCA	HIF1A	JUN	MRE11A	PDPK1	RNF43	SP140	VHL
ALK	BCR	CRBN	FANCC	HIST1H1B	KDM5A	MSH2	PDS5B	ROBO1	SPEN	WHSC1
ALOX12B	BIRC3	CREBBP	FANCD2	HIST1H1C	KDM5C	MSH6	PHF6	ROS1	SPOP	WT1
AMER1	BLM	CRKL	FAS	HIST1H1D	KDM6A	MTOR	PIGA	RPTOR	SRC	XBP1
APC	BRAF	CRLF2	FAT1	HIST1H1E	KDR	MUTYH	PIK3C2G	RRAGC	SRSF2	XPO1
AR	BRCA1	CSF1R	FBXO11	HIST1H2AC	KEAP1	MYC	PIK3C3	RTEL1	STAG1	ZRSR2
ARAF	BRCA2	CSF3R	FBXW7	HIST1H2AG	KIT	MYCL1	PIK3CA	RUNX1	STAG2	
ARHGEF28	BRD4	CTCF	FGF19	HIST1H2AL	KMT2A	MYCN	PIK3CG	RUNX1T1	STAT3	
ARID1A	BRIP1	CTNNB1	FGF3	HIST1H2AM	KMT2B	MYD88	PIK3R1	SAMHD1	STAT5A	
ARID1B	BTG1	CUX1	FGF4	HIST1H2BC	KMT2C	NBN	PIK3R2	SDHA	STAT5B	
ARID2	BTK	CXCR4	FGFR1	HIST1H2BD	KMT2D	NCOR1	PIM1	SDHB	STAT6	
ARID3A	CALR	CYLD	FGFR2	HIST1H2BG	KRAS	NCOR2	PLCG1	SDHC	STK11	
ARID3B	CARD11	DAXX	FGFR3	HIST1H2BJ	KSR2	NCSTN	PLCG2	SDHD	SUFU	
ARID3C	CASP8	DDR2	FGFR4	HIST1H2BK	LCK	NF1	PMS2	SETBP1	SUZ12	
ARID4A	CBFB	DDX3X	FLCN	HIST1H2BO	LMO1	NF2	PNRC1	SETD1A	SYK	
ARID4B	CBL	DIS3	FLT1	HIST1H3B	LTB	NFE2	POT1	SETD1B	TBL1XR1	
ARID5A	CCND1	DNMT3A	FLT3	HIST1H3G	MALT1	NFE2L2	PPP2R1A	SETD2	TBX3	
ARID5B	CCND2	DOT1L	FLT4	HLA-A	MAP2K1	NKX2-1	PRDM1	SETD3	TERT	
ASXL1	CCND3	DTX1	FOXL2	HNF1A	MAP2K2	NOTCH1	PRKAR1A	SETD4	TET1	
ASXL2	CCNE1	DUSP22	FOXO1	HRAS	MAP2K4	NOTCH2	PTCH1	SETD5	TET2	
ATM	CD274	EED	FOXP1	ID3	MAP3K1	NOTCH3	PTEN	SETD6	TET3	
ATP6AP1	CD28	EGFR	FURIN	IDH1	MAP3K13	NOTCH4	PTPN1	SETD7	TGFBR2	
ATP6V1B2	CD58	EGR1	FYN	IDH2	MAP3K14	NPM1	PTPN11	SETD8	TNFAIP3	
ATR	CD79A	EP300	GATA1	IGF1	MAPK1	NRAS	PTPN2	SETDB1	TNFRSF14	
ATRX	CD79B	EP400	GATA2	IGF1R	MAPK3	NSD1	RAD21	SETDB2	TOP1	
ATXN2	CDC73	EPHA3	GATA3	IGF2	MCL1	NT5C2	RAD50	SF3B1	TP53	
AURKA	CDH1	EPHA5	GNA11	IKBKE	MDM2	NTRK1	RAD51	SGK1	TP63	
AURKB	CDK12	EPHA7	GNA12	IKZF1	MDM4	NTRK2	RAD51B	SH2B3	TRAF2	
AXIN1	CDK4	EPHB1	GNA13	IKZF3	MED12	NTRK3	RAD51C	SMAD2	TRAF3	
AXL	CDK6	ERBB2	GNAQ	IL7R	MEF2B	P2RY8	RAD51D	SMAD4	TRAF5	
B2M	CDK8	ERBB3	GNAS	INPP4B	MEN1	PAK7	RAD52	SMARCA4	TSC1	

BACH2	CDKN1B	ERBB4	GNB1	IRF1	MET	PALB2	RAD54L	SMARCB1	TSC2
BAP1	CDKN2A	ERG	GRIN2A	IRF4	MGA	PARP1	RAF1	SMARCD1	TSHR
BARD1	CDKN2B	ESCO2	GSK3B	IRF8	MGAM	PAX5	RARA	SMC1A	TYK2
BCL10	CDKN2C	ESR1	GTF2I	IRS2	MITF	PBRM1	RB1	SMC3	U2AF1

Table S7 Gene list of Archer panel

ABL1	CCND3	KAT6A	NUP214	RUNX1
ABL2	CDK6	KMT2A	P2RY8	RUNX1T1
ALK	CHIC2	MECOM	PDGFRA	STIL
BCL2	CRLF2	MKL1	PDGFRB	TAL1
BCL6	DEK	MLF1	PICALM	TCF3
BCR	DUSP22	MLLT10	PML	TP63
BIRC3	ETV6	MYC	PRDM16	
CBFB	FGFR1	MYH11	RARA	
CCND1	JAK2	NOTCH1	RBM15	