

Supplemental data

(Each table should be a separate excel file.)

Table S1

Co-occurrence status of *H3K27M* and *IDH2* mutations in TARGET-AML and BEAT-AML.

Identification of 9 pAML patients that harbored K27M mutation on Histone 3 genes based on evidence of VAF > 0.15 and total read depth > 8 and whether the mutation can be captured by both RNA-seq and WGS data.

Co-occurrence of *H3F3A* (H3.3) *K27M* and *IDH2* *R172K* are shown in 2 pAML patients. Co-occurrence of *H3K27M* (H3.3 & H3.1) and *IDH2* *R140Q/R172K* are shown in 5 adult AML patients.

	CASE_ID	SYMBOL	H3K27M				IDH2				
			DNA-vaf-T1	DNA-vaf-T2	RNA-vaf-T1	RNA-vaf-T2	SYMBOL	DNA-vaf-T1	DNA-vaf-T2	RNA-vaf-T1	RNA-vaf-T2
H3.3	PARBTV	H3F3A	47%	48%	47%	47%	R172K	38%	48%	56%	59%
	PAVDMY	H3F3A			49%	47%/47%	R172K			39%	40%/48%
H3.1	PAPVGE	HIST1H3C			58%		-			-	
	PAUZTH	HIST1H3J(K27I)			0%	38%	-			-	-
	PAUUPR	HIST1H3I			0%	35%	-			-	-
	PAKWCU	HIST1H3D			17%		-			-	
	PAXFAG	HIST1H3C			54%		-			-	
	PAXKAL	HIST1H3I			50%		-			-	
	PATFGK	HIST1H3C			50%		-			-	

	CASE_ID	SYMBOL	H3K27M			IDH2			
			DNA-vaf	RNA-vaf	TS-vaf	SYMBOL	DNA-vaf	RNA-vaf	TS-vaf
H3.3	2148	H3F3A	29%	47%		R140Q	40%	52%	
H3.1	2354	HIST1H3C	34%/33%	low-exp		R172K	36%/31%	47%	
	2429	HIST1H3B	33%/47%	35.29%/100%		-	-	-	
	2498	HIST1H3C	37%	38%		R140Q	48%	47%	
	2530	HIST1H3	40%	low-exp		R172K	46%	49%	

		B							
	2611	HIST1H3 D		58%	39%	-		-	-
	2721	HIST1H3 B			36%	R172K			36%

Table S2

H3K27 variants: published work (n=1049) and TARGET/BEAT-AML cohorts (n = 2934, via bamSliceR).
 Lehnertz et al. *Blood* 2017 documented 2 adult AML patients. Boileau et al. *Nat Commun* 2019 documented 4 adult AML patients. We documented 16 AML patients from TARGET and BEAT AML cohorts.

Cohort	Cohort Size (n)	WGS/WXS (n)	RNAseq (n)	DNA Methylation (n)	H3K27M/I (%/n)
Lehnertz et al. <i>Blood</i> (2017)					
Leucegene	415		415		0.48%/2
Boileau et al. <i>Nat Commun</i> (2019)					
Toronto	312	312			0.64%/2
Lebanon	122	122			0.8%/1
TCGA	200	200	200	200	0.5%/1
Identification of H3K27M in BEAT-AML and TARGET-AML					
TARGET 20/21	2045	365	2281	2000	0.4%/9
Beat-AML	826	798	653		0.8%/7

Table S3

Human *MLLT1* YEATS domain insertion/deletion variants identified in the pan-TARGET cohort.

Chromosome	POS	SYMBOL	AAchange	REFCODON	VARCODON	REFAA	VARAA	alt_count	total_count	VAF	patient_id
chr19	6230649	MLLT1	V114VNHL	GTG	GTGAACC ACCTG	V	VNHL	5	51	0.09804	PASBGZ
chr19	6230642	MLLT1	H116HLRP	CAC	CACCTGC GCCCC	H	HLRP	2	460	0.00435	PANGJY
chr19	6230645	MLLT1	N115NPLR	AAC	AACCCCC TGCGC	N	NPLR	4	470	0.00851	PANGJY
chr19	6230645	MLLT1	N115NHLR	AAC	AACCACC TGCGC	N	NHLR	55	470	0.11702	PANGJY
chr19	6230640	MLLT1	HL116L	CACCTG	CTG	HL	L	2	134	0.01493	PALHVV
chr19	6230646	MLLT1	N115NHLH	AAC	AACCACC TGCAC	N	NHLH	2	76	0.02632	PASBPK
chr19	6230582	MLLT1	LL135L	CTCCTG	CTG	LL	L	2	175	0.01143	PAUMUZ
chr19	6230611	MLLT1	NP126P	AACCCC	CCC	NP	P	2	370	0.00541	PAUHGM
chr19	6230616	MLLT1	TFN123N	ACCTTCA AC	AAC	TFN	N	2	48	0.04167	PAWVPZ
chr19	6230620	MLLT1	TF123F	ACCTTC	TTC	TF	F	2	690	0.00290	PAVDXR
chr19	6230574	MLLT1	AG138G	GCCGGC	GGC	AG	G	2	175	0.01143	PABYYR
chr19	6230570	MLLT1	GG139G	GCGGGG	GGG	GG	G	2	1047	0.00191	PAUWZR

Figure S1

VAF distribution of DNMT3A variants.

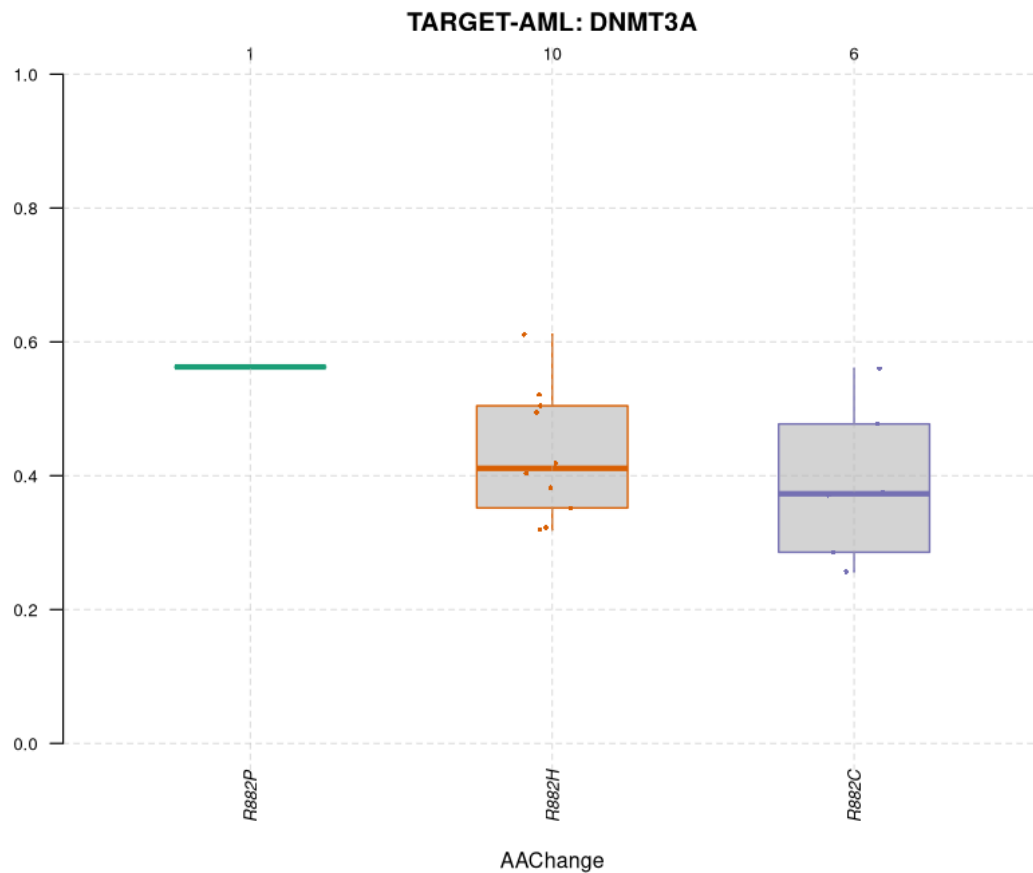


Figure S2

VAF distribution of H3K27 variants.

