

Supplementary Material

Genomic and transcriptomic determinants of clinical outcomes in patients with AML and *DNMT3A* mutations

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Supplementary Methods

Subjects

We enrolled 884 newly diagnosed patients with *de novo* AML at the National Taiwan University Hospital (NTUH). To focus on a more homogeneous group of patients with AML, those with antecedent hematological diseases, history of cytopenia, family history of myeloid neoplasms or therapy-related AML were excluded. All patients received standard induction chemotherapy and consolidation. The consolidation chemotherapy was 2-4 courses of high-dose cytarabine (2000 mg/m² every 12 hours for days 1-4, total 8 doses), with or without one anthracycline idarubicin (12 mg/m²) or mitoxantrone (12 mg/m²). Among the 378 patients who underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT), 183 (48.9%) received allo-HSCT in CR1. The choice of allo-HSCT for patients afflicted with AML at our institute is largely based on chromosomal results, mutation data, age, availability of HLA-matched donors as well as the response to induction treatment.

Supplementary Figures

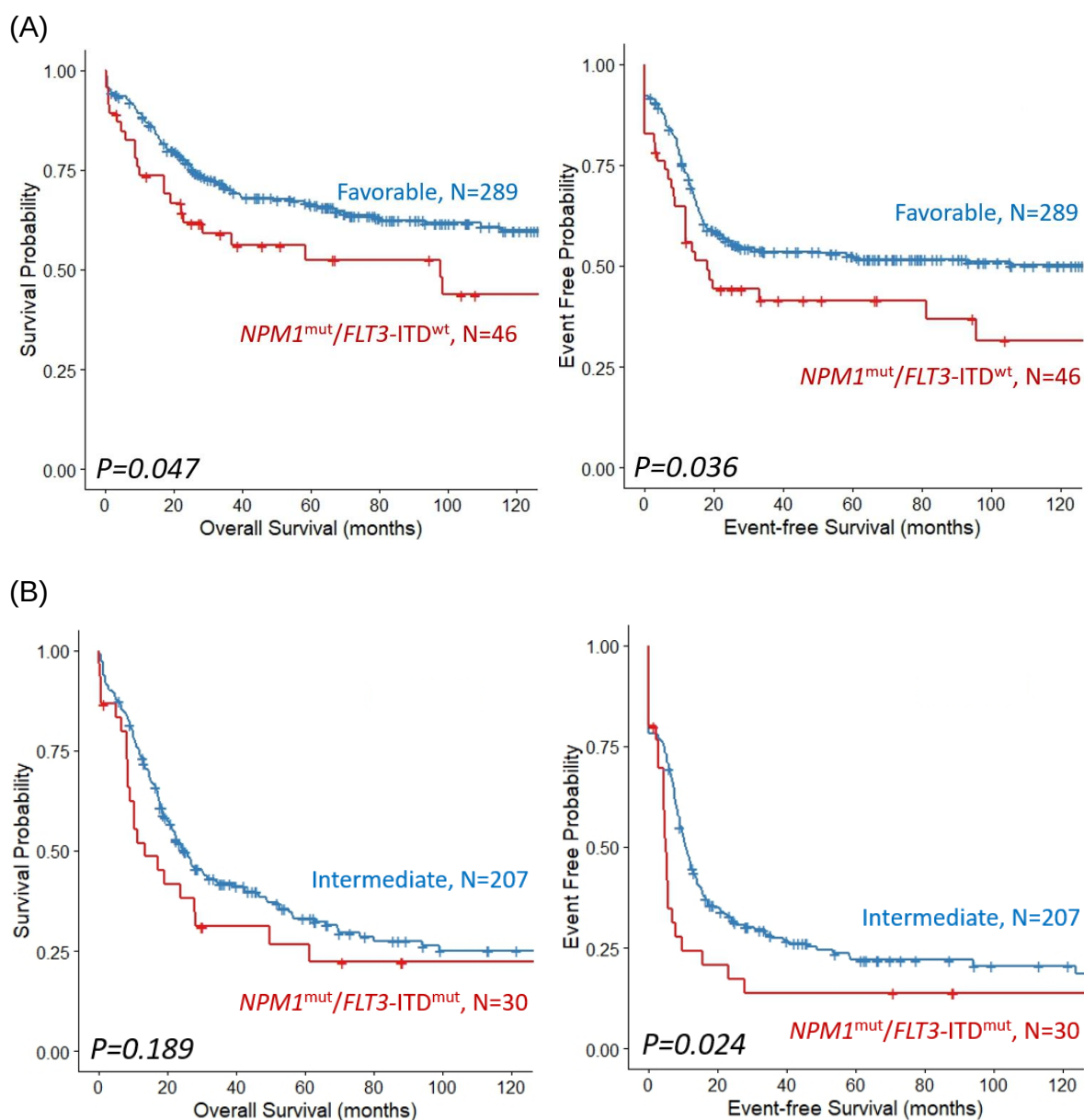
Supplementary Figure 1

OS and EFS in *DNMT3A*-mutated patients stratified by *NPM1* and *FLT3*-ITD statuses, with comparison to current ELN-2022 risk categories

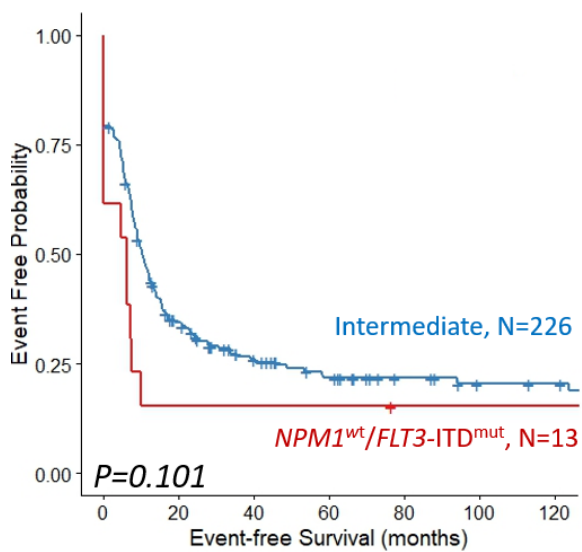
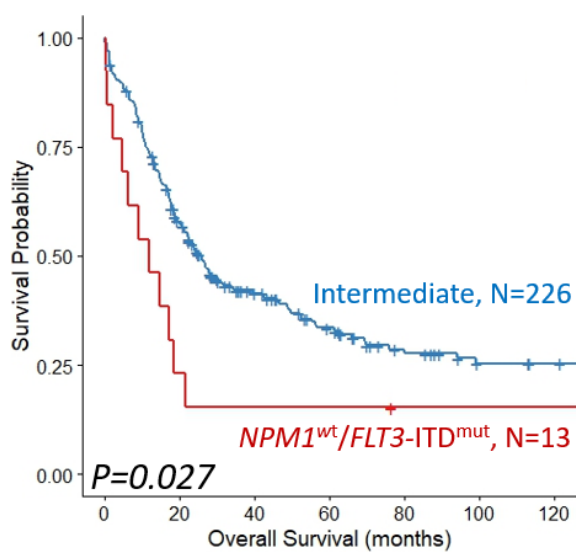
(A) Patients with *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt} exhibited inferior OS and EFS compared to the ELN-2022 favorable-risk group.

(B) Patients with *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{mut} exhibited inferior EFS compared to the ELN-2022 intermediate-risk group.

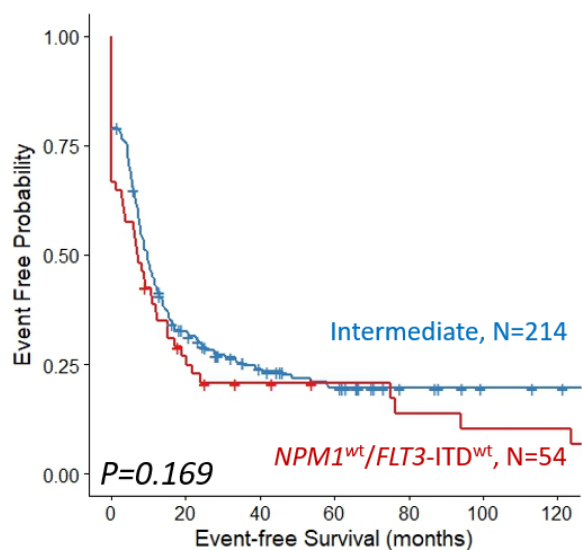
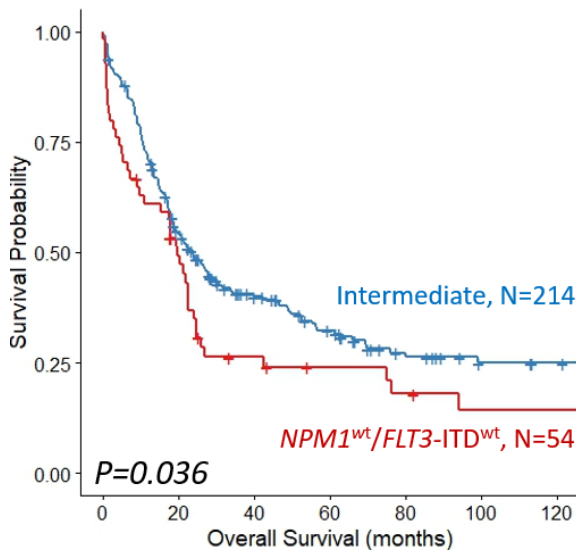
(C, D) Patients with *DNMT3A*^{mut}/*NPM1*^{wt}/*FLT3*-ITD^{mut} and *DNMT3A*^{mut}/*NPM1*^{wt}/*FLT3*-ITD^{wt} exhibited inferior OS compared to the ELN-2022 intermediate-risk group.



(C)



(D)

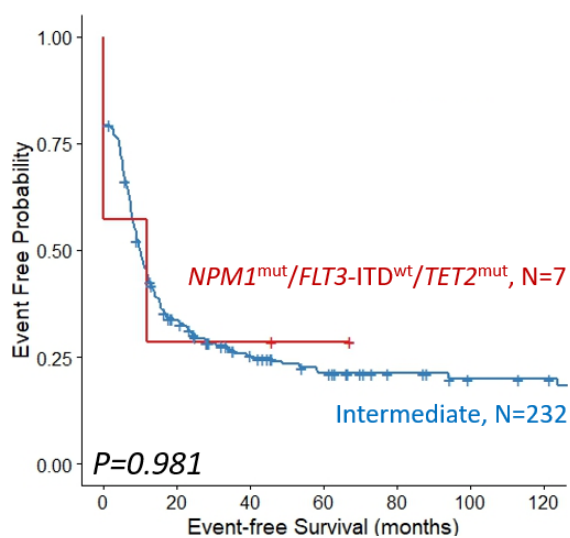
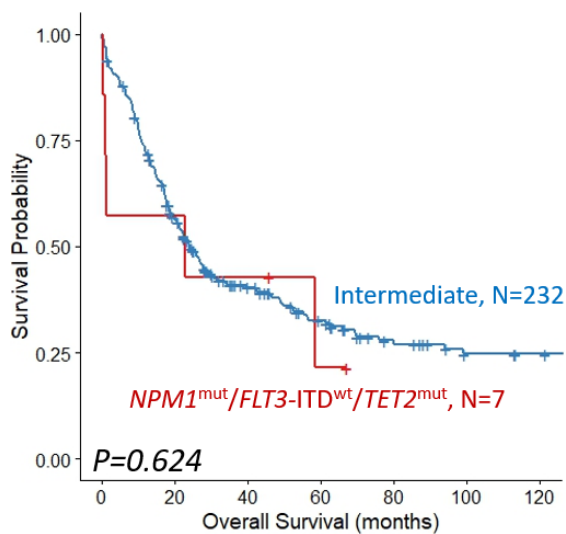


Supplementary Figure 2

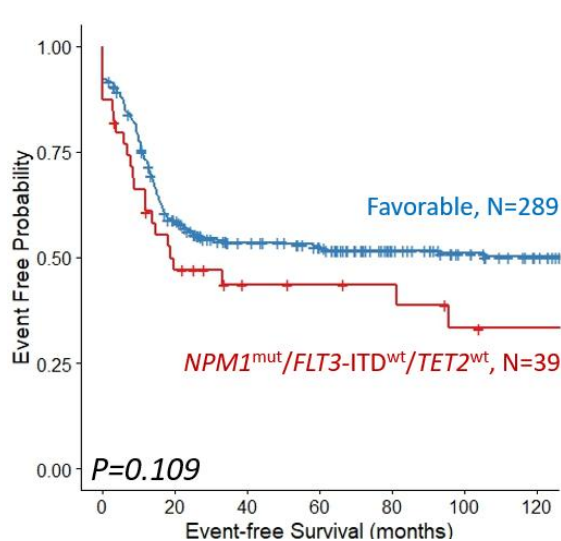
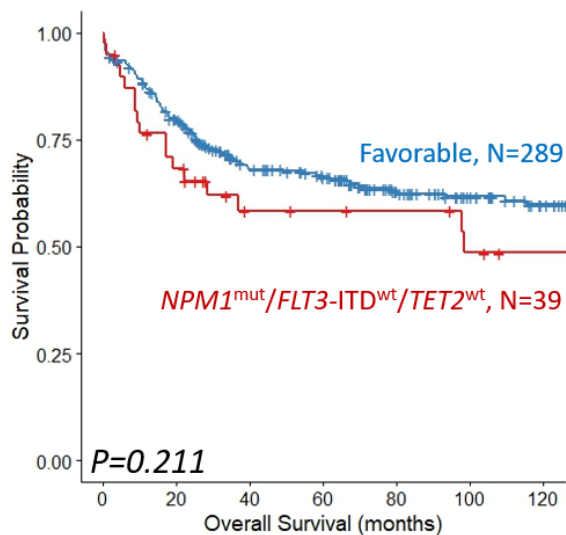
OS and EFS in *DNMT3A*-mutated patients stratified by *NPM1* and *FLT3*-ITD statuses and co-mutations

- (A) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt}/*TET2*^{mut} subgroup compared to the ELN-2022 intermediate-risk group.
- (B) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt}/*TET2*^{wt} subgroup compared to the ELN-2022 favorable-risk group.
- (C) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt} subgroup stratified by *TET2* mutation status. There was a trend towards worse outcomes in the *TET2*-mutated group.
- (D) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt}/*PTPN11*^{wt}/*IDH2*^{wt} subgroup stratified by *TET2* mutation status. The presence of *TET2* mutations in this subgroup was associated with significantly worse OS and a trend toward worse event-free survival.
- (E) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{mut} subgroup stratified by co-mutations: signaling pathway mutations (*PTPN11*, *FLT3*-TKD, and *NRAS*), myeloid dysplasia related genes (MDS-R) mutations (*ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1*, and *ZRSR2*) and total subgroup patients.
- (F) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{wt}/*FLT3*-ITD^{mut} subgroup stratified by co-mutations: MLL-PTD, MDS-R mutations and total subgroup patients.
- (G) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{wt}/*FLT3*-ITD^{wt} subgroup stratified by co-mutations: *NRAS*, *IDH2*, MDS-R mutations and total subgroup patients.
- (H) OS and EFS in the *DNMT3A*^{mut}/*NPM1*^{wt}/*FLT3*-ITD^{wt}/*IDH2*^{wt} stratified by *NRAS* mutations status. The presence of *NRAS* mutations in this subgroup was associated with significantly better OS.

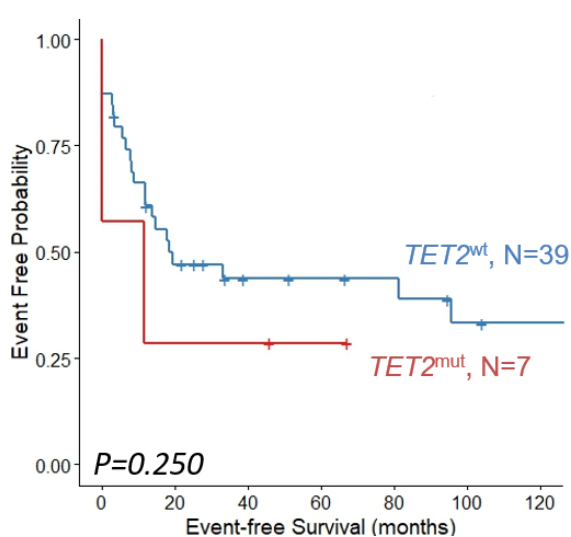
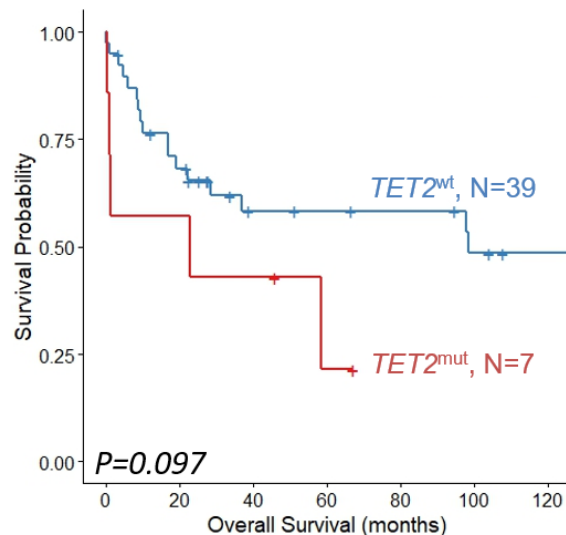
(A)



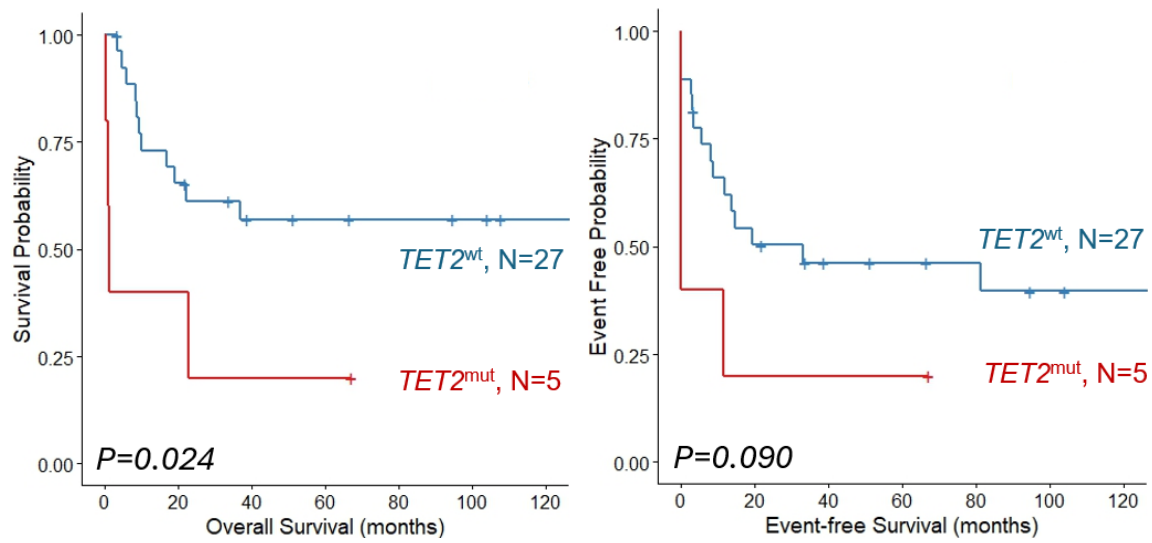
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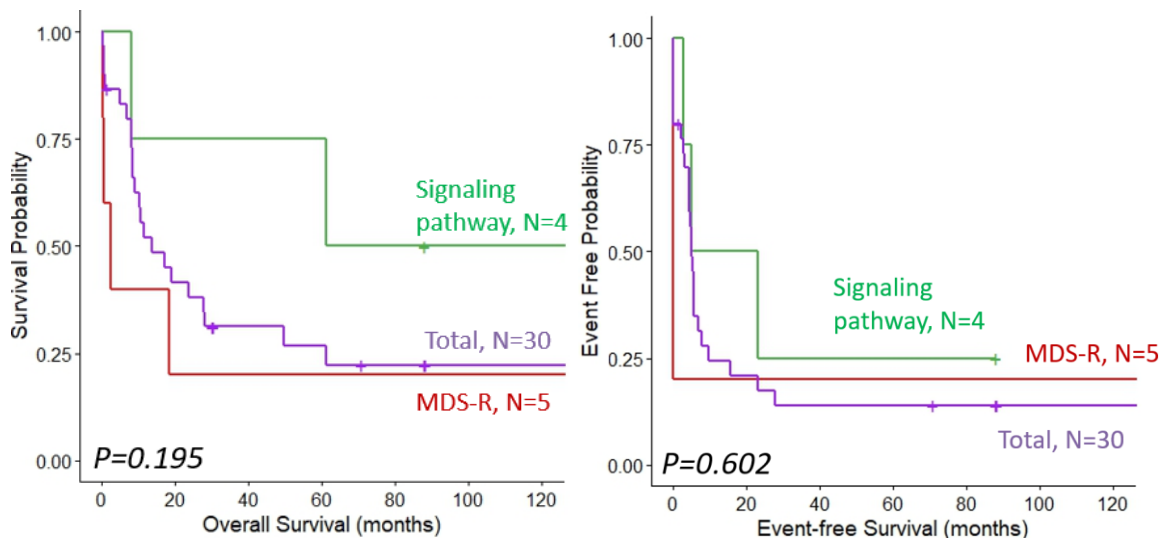
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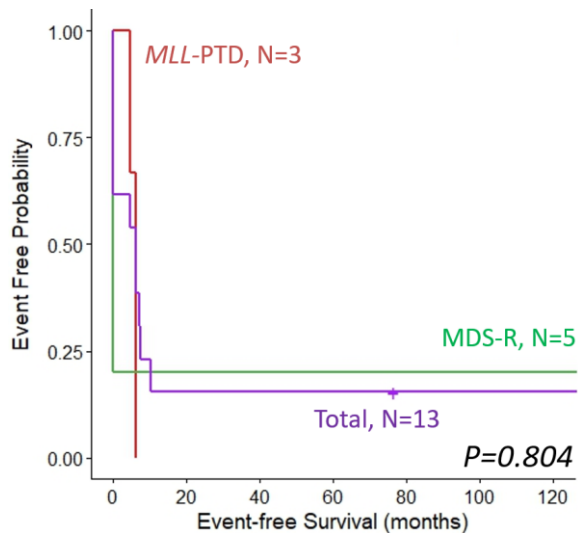
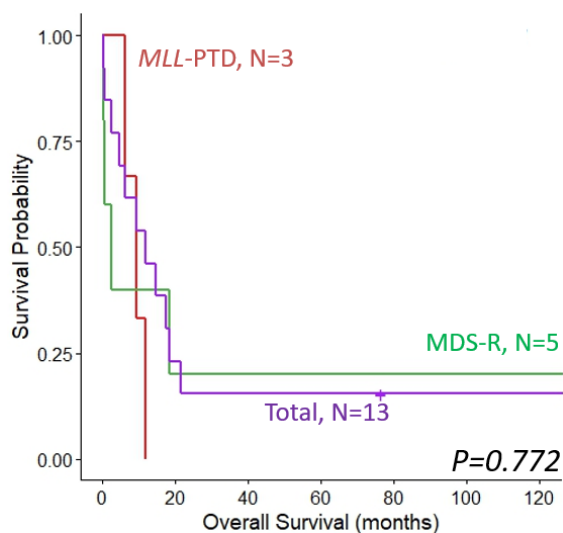
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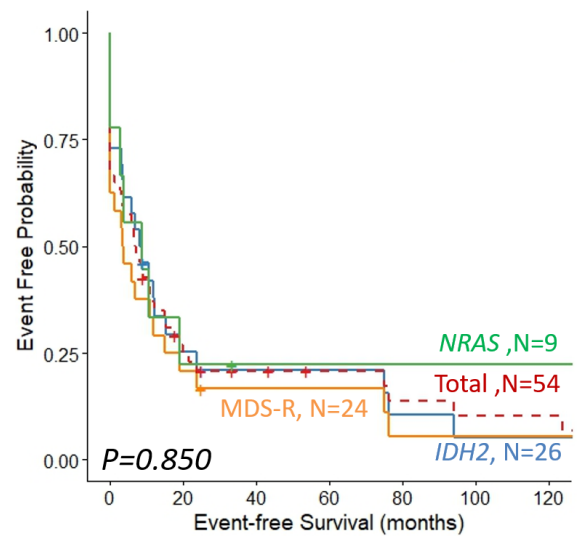
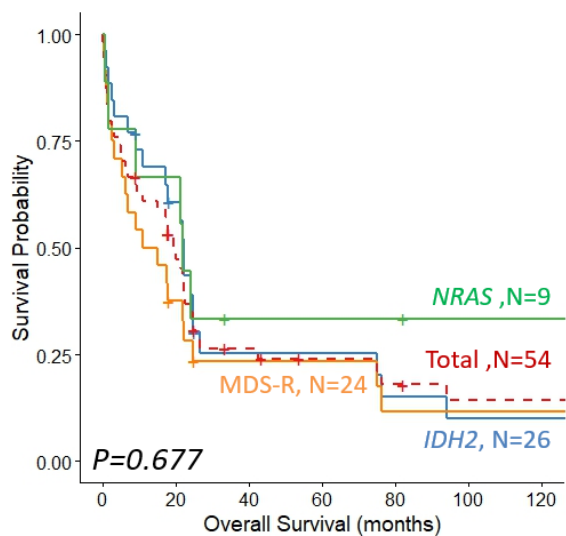
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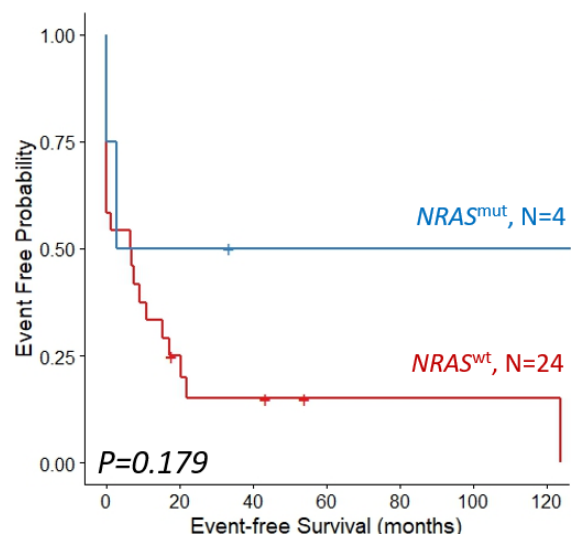
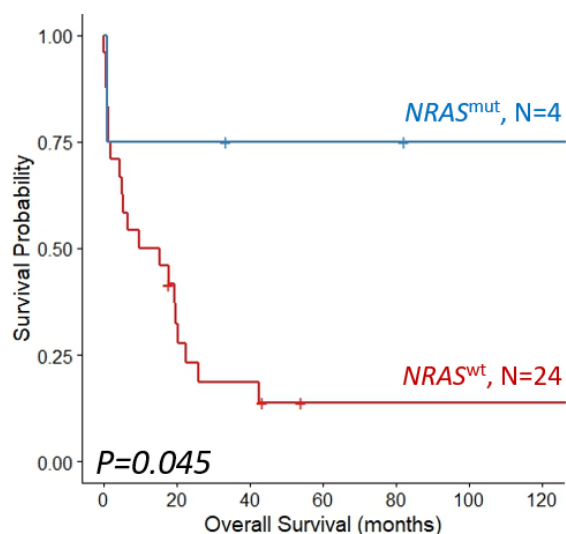
(F)



(G)



(H)

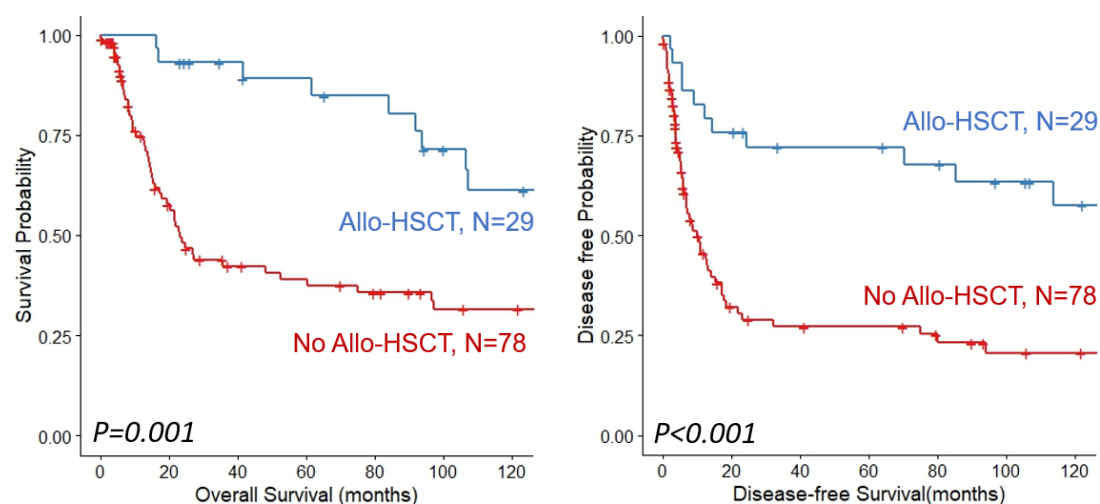


Supplementary Figure 3

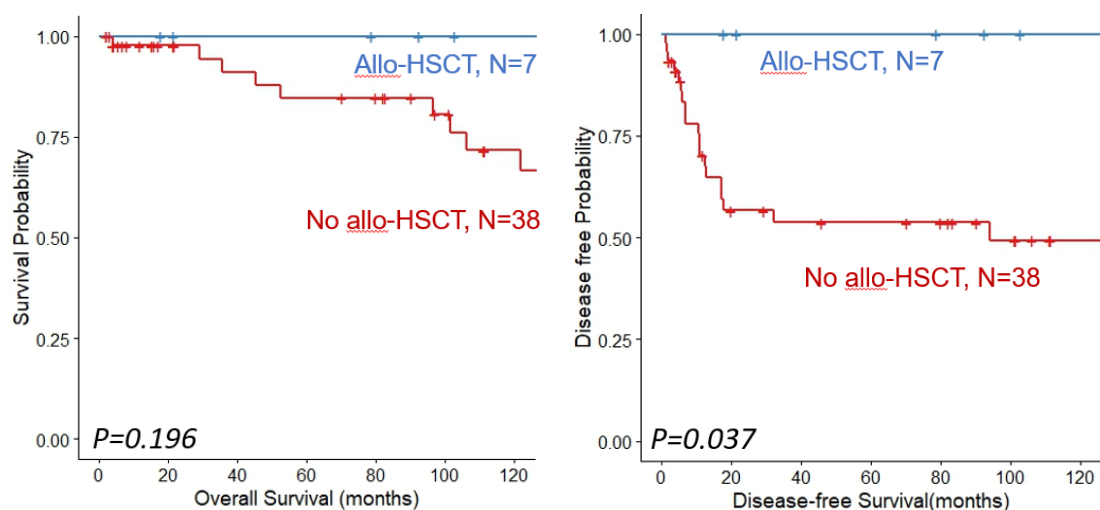
Prognostic impact of allo-HSCT at CR1 in *DNMT3A*^{mut} AML patients

(A) *DNMT3A*^{mut} AML patients at CR1 who received allo-HSCT demonstrated significantly improved OS and DFS. (B) *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt} AML patients at CR1 who received allo-HSCT demonstrated significantly improved DFS and a trend toward better OS.

(A)



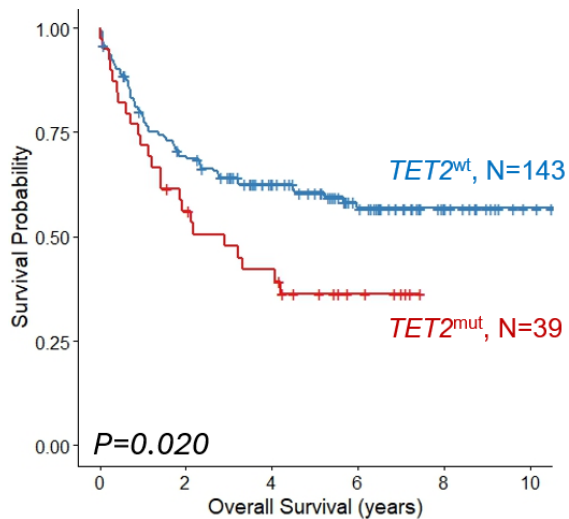
(B)



Supplementary Figure 4

External Validation of survival outcome stratified by co-mutations in AML with *DNMT3A*^{mut}

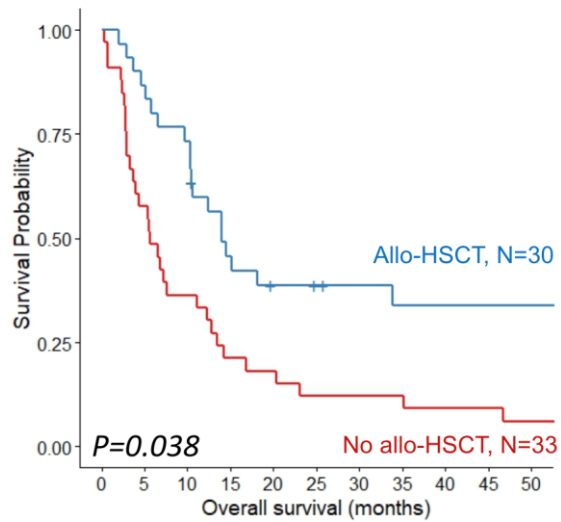
OS in the combined AMLSG and UK-NCRI cohorts for the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt}/*PTPN11*^{wt}/*IDH2*^{wt} subgroup, stratified by *TET2* mutation status. The presence of *TET2* in this subgroup showed significantly worse OS.



Supplementary Figure 5

Clinical outcomes of patients with *DNMT3A*^{mut} with relapse

Allo-HSCT after relapse had significantly better OS compared with those without allo-HSCT.

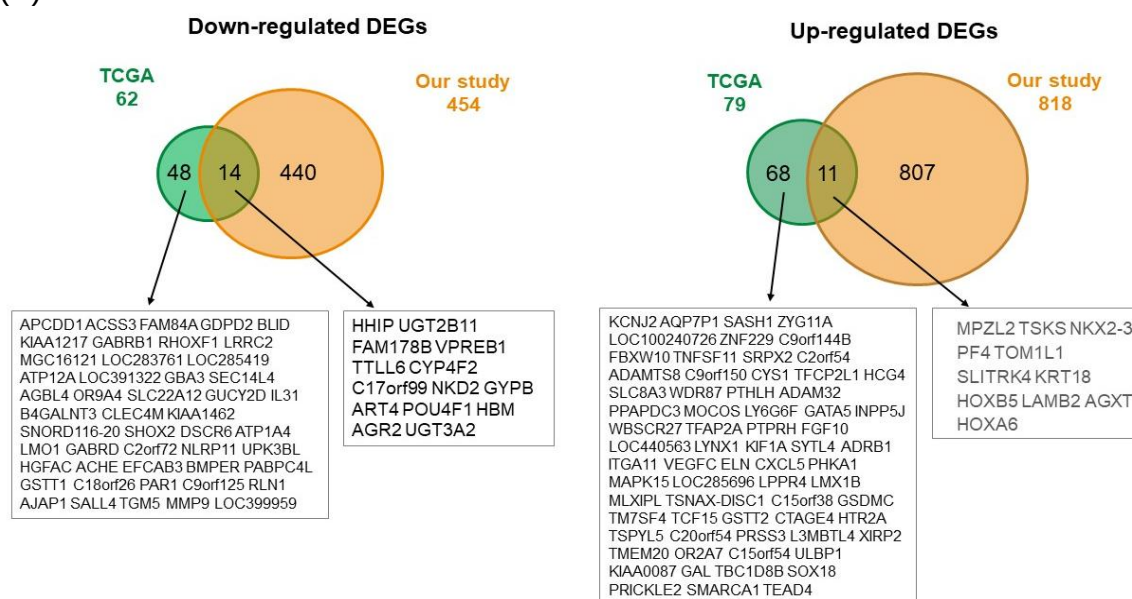


Supplementary Figure 6

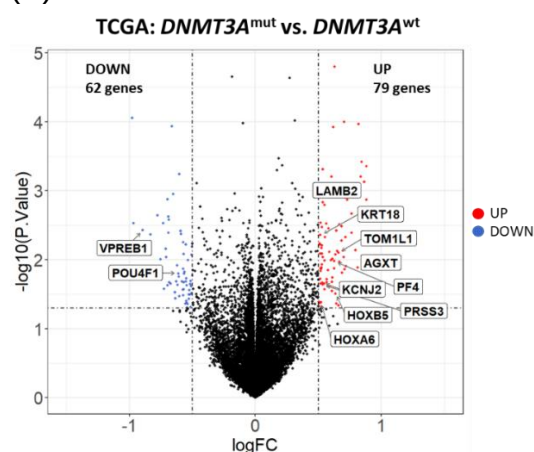
Transcriptional signatures in patients with *DNMT3A*^{mut} compared with *DNMT3A*^{wt} in TCGA cohort

- (A) Venn diagram depicting the DEGs identified in our study and the TCGA cohort when comparing the RNA-seq data between *DNMT3A*^{mut} and *DNMT3A*^{wt} patients.
- (B) Volcano plot displaying all genes from the RNA-seq comparison between *DNMT3A*^{mut} and *DNMT3A*^{wt} patients. A positive fold change ($\log_{2}FC > 0$) indicated upregulated genes, and a negative fold change ($\log_{2}FC < 0$) indicated downregulated genes in *DNMT3A*^{mut} patients.
- (C) Bubble plots illustrating enriched and depleted MSigDB CGP and Hallmark gene sets between *DNMT3A*^{mut} and *DNMT3A*^{wt}.
- (D) GSEA enrichment plots showing significant enrichment of immune gene set signatures and *NPM1*-mutated AML signatures within the *DNMT3A*^{mut} transcriptome.

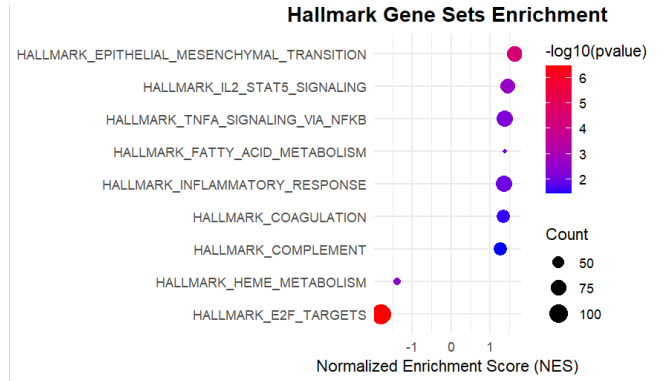
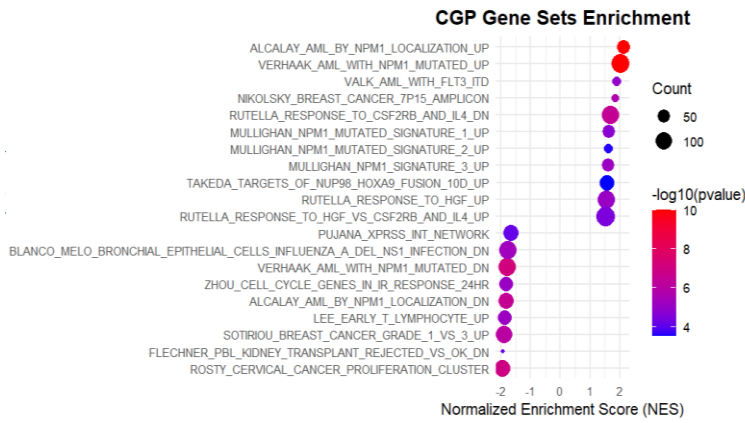
(A)



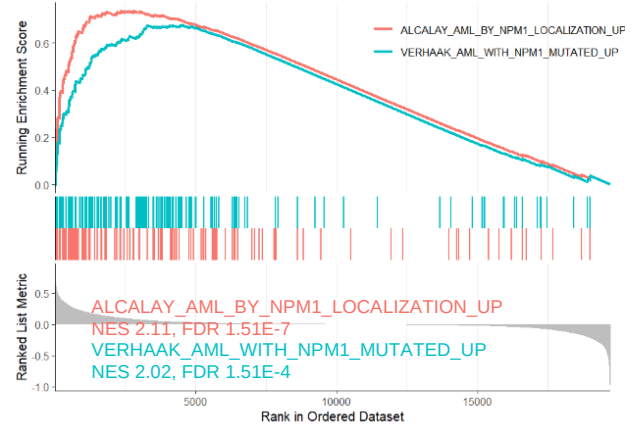
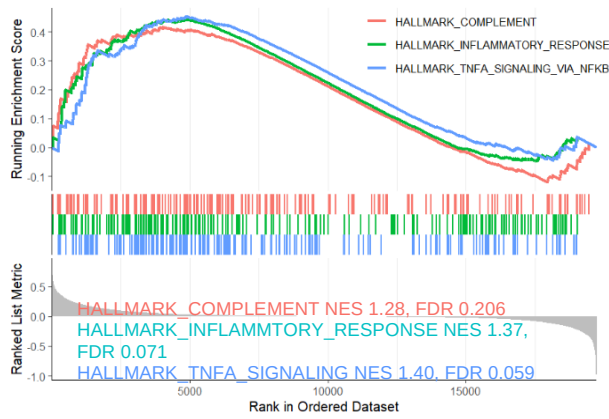
(B)



(C)



(D)

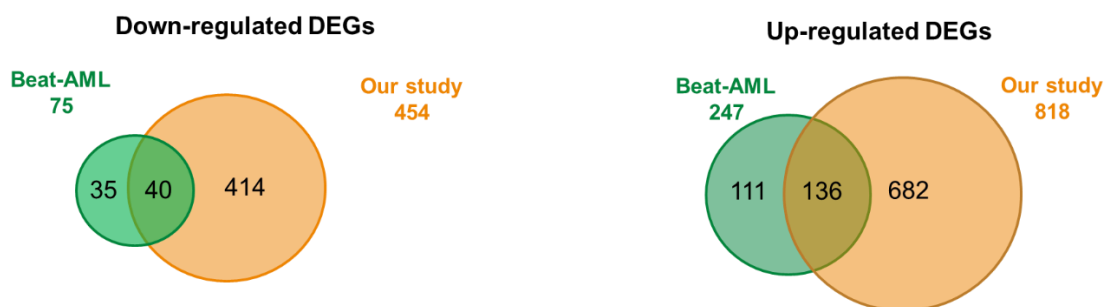


Supplementary Figure 7

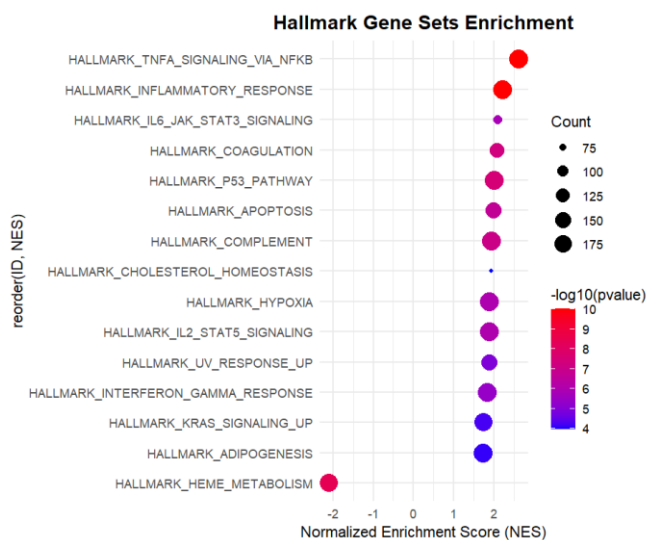
Transcriptional signatures in patients with *DNMT3A*^{mut} compared with *DNMT3A*^{wt} in Beat-AML cohort

- (A) Venn diagram depicting the DEGs identified in our study and the Beat-AML cohort when comparing the RNA-seq data between *DNMT3A*^{mut} and *DNMT3A*^{wt} patients.
- (B) Bubble plots illustrating enriched and depleted MSigDB Hallmark gene sets between *DNMT3A*^{mut} and *DNMT3A*^{wt} in the Beat-AML cohort. Bubble size represented the gene counts, while color indicated statistical significance.

(A)



(B)



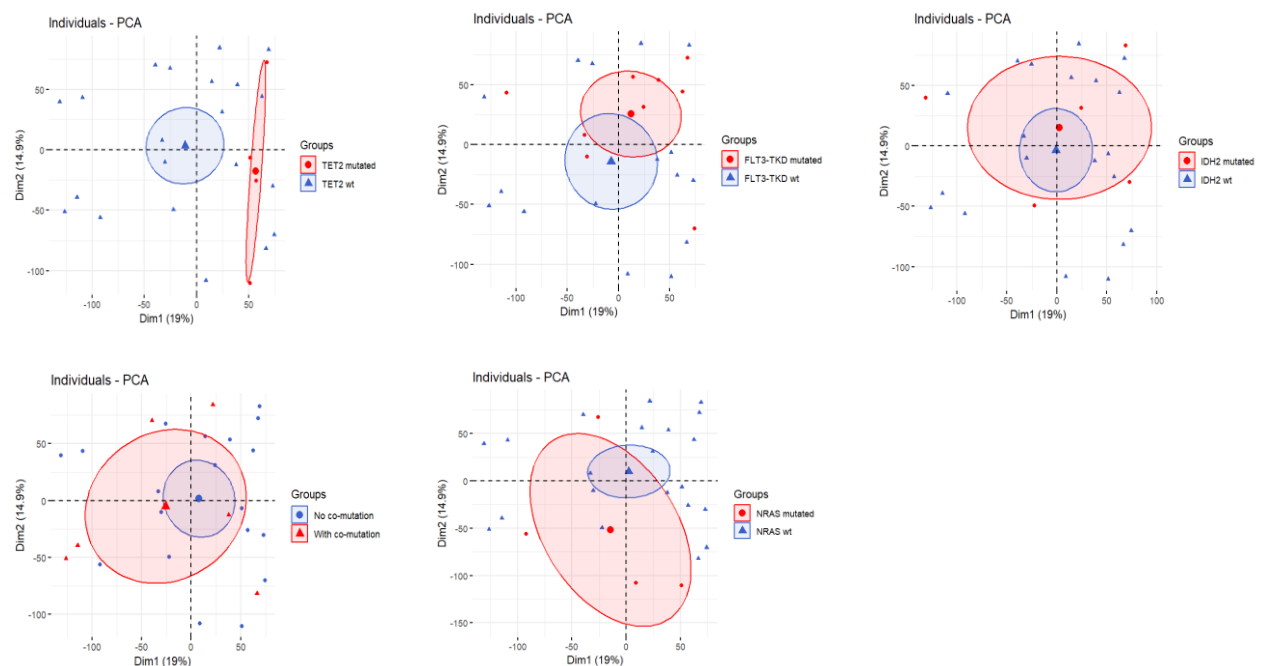
Supplementary Figure 8

Differential transcriptional signatures between *TET2*^{mut} and *TET2*^{wt} AML within the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt} subgroup in our cohort

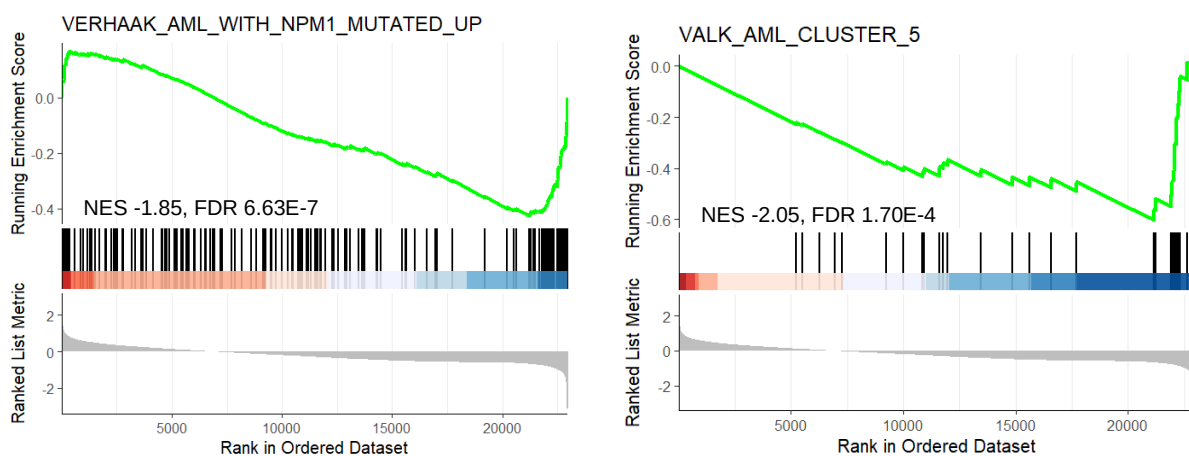
(A) PCA clustering of transcriptomes between AML within the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt} subgroup, stratified by the presence or absence of *TET2*, *FLT3*-TKD, *IDH2*, *NRAS* and any co-mutations.

(B) GSEA enrichment plots showing significant enrichment of selected AML signatures within the *TET2*^{mut} transcriptome

(A)



(B)

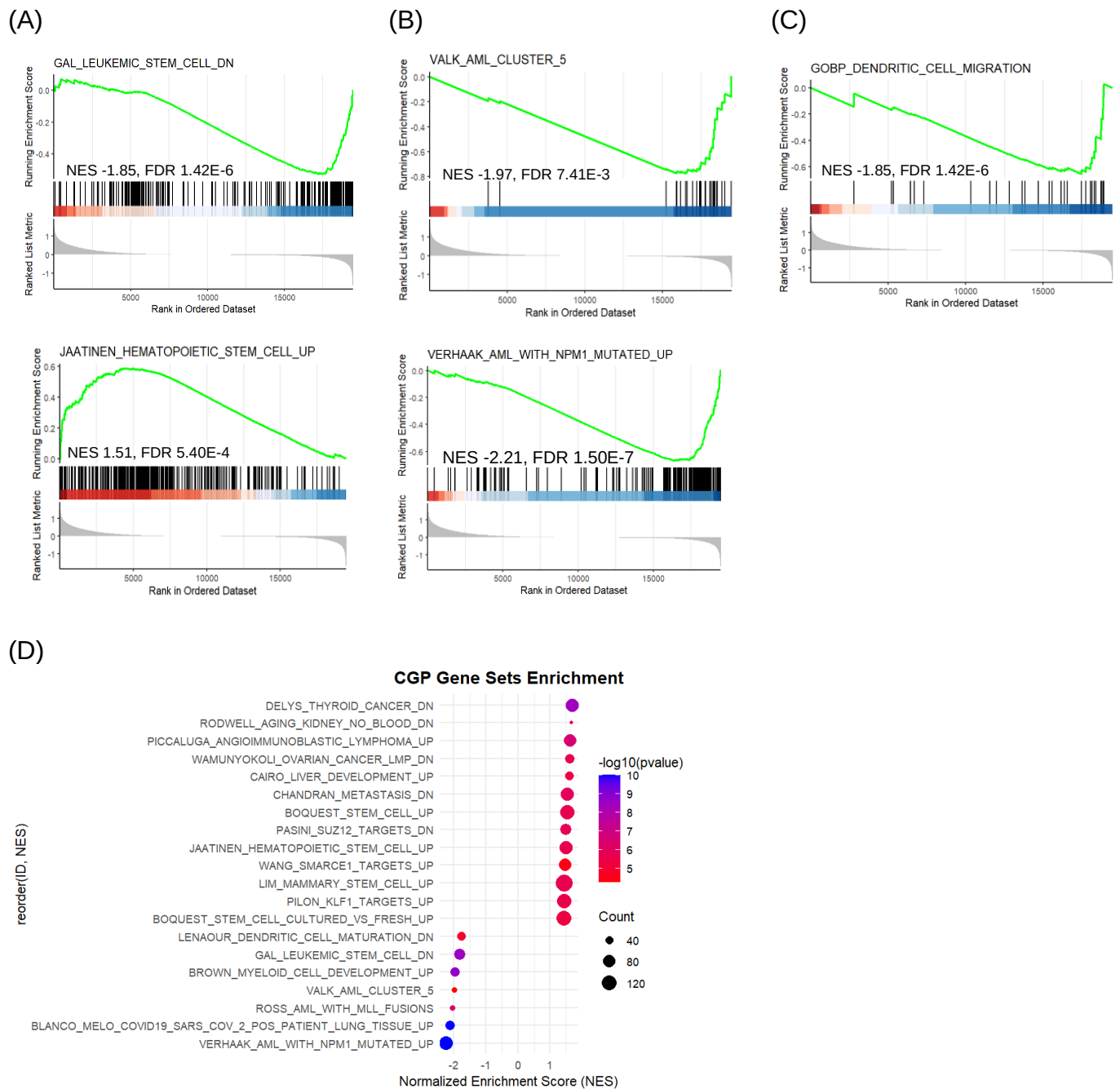


Supplementary Figure 9

Differential transcriptional signatures between *TET2*^{mut} and *TET2*^{wt} AML within the *DNMT3A*^{mut}/*INPM1*^{mut}/*FLT3*-ITD^{wt} subgroup in TCGA cohort

(A-C) GSEA enrichment plots showing significant enrichment of LSC signatures, selected AML signatures, and pathways associated with dendritic cell migration within the *TET2*^{mut} group.

(D) Bubble plot illustrating enriched and depleted MSigDB CGP gene sets between *TET2*^{mut} and *TET2*^{wt}.



Supplementary Tables

Supplementary Table 1. Characterization of the mutations of *DNMT3A*^{mut} AML patients

Supplementary Table 1 is available in the supplementary files.

Supplementary Table 2. Comparison of other genetic alterations between patients with AML according to their *DNMT3A* statuses

	Total pts Examined	Whole cohort (%)	<i>DNMT3A</i> ^{wt}	<i>DNMT3A</i> ^{mut}	P value
Activated signaling					
<i>FLT3</i> -ITD	879	17.9	15.4	30.6	<0.001
<i>FLT3</i> -TKD	877	8.0	6.6	15.3	<0.001
<i>NRAS</i>	880	14.7	15.0	13.2	0.580
<i>KRAS</i>	879	4.9	5.0	4.2	0.673
<i>PTPN11</i>	877	5.0	4.0	9.7	0.004
<i>KIT</i>	797	5.5	6.3	1.4	0.017
<i>JAK2</i>	817	0.9	1.1	0	0.456
<i>CBL-b</i>	863	0	0	0	-
<i>c-CBL</i>	863	0.8	0.8	0.7	0.886
Transcription factors					
<i>RUNX1</i>	876	11.1	11.7	7.6	0.151
<i>GATA2</i>	870	7.8	8.6	3.5	0.034
<i>ETV6</i>	860	1.8	1.8	2.1	0.786
DNA methylation					
<i>TET2</i>	875	10.7	10.9	9.7	0.668
<i>IDH1</i>	877	5.0	4.0	10.4	0.001
<i>IDH2</i>	877	11.8	9.0	26.4	<0.001
<i>WT1</i>	877	8.0	8.5	5.6	0.234
Chromatin modifiers					
<i>ASXL1</i>	877	9.8	10.1	8.3	0.510
<i>EZH2</i>	861	1.0	1.1	0.7	0.673
<i>KMT2A</i> -PTD	879	3.1	3.0	3.5	0.748
<i>SETBP1</i>	567	1.8	1.8	2.1	0.786
<i>BCOR</i>	861	1.9	1.6	3.5	0.138
<i>PHF6</i>	860	2.1	2.4	0.7	0.189
Splicing					
<i>SF3B1</i>	871	2.6	2.7	2.1	0.671
<i>U2AF1</i>	871	3.8	4.2	2.1	0.230
<i>SRSF2</i>	872	4.1	4.0	4.2	0.948
<i>ZRSR2</i>	556	1.5	0.9	4.2	0.003
Cohesin genes	860	5.4	5.3	6.3	0.632
<i>STAG1</i>	866	0.3	0.4	0	0.444
<i>STAG2</i>	865	3.8	3.8	4.2	0.825
<i>RAD21</i>	866	2.5	2.2	4.2	0.157
<i>SMC1</i>	867	2.1	1.9	3.5	0.230
<i>SMC3</i>	866	1.0	0.8	2.1	0.163
<i>NPM1</i>	880	19.5	13.1	52.8	<0.001
<i>TP53</i>	877	5.3	6.0	2.1	0.059

CEBPA	885	16.0	13.5	1.4	<0.001
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Supplementary Table 3

Characteristics of 29 *DNMT3A* mutation patients who received allogeneic hematopoietic stem cell transplantation at CR1

UPN	Age	Cytogenetics	Co-Mutations	HSCT Indication	<i>NPM1</i> PCR status before HSCT	Transplant type	Relapsed after HSCT
2	35	NK	<i>FLT3</i> -ITD, <i>ZRSR2</i>	Adverse genetic mutation	Nil	Matched sibling	No
161	36	NK	<i>NRAS</i> , <i>IDH1</i>	AML intermediate risk	Nil	Matched sibling	No
236	33	NK	<i>NPM1</i> , <i>FLT3</i> -TKD	Delayed CR1	ND	Matched sibling	No
265	38	NK	<i>NPM1</i> , <i>FLT3</i> -ITD, <i>IDH1</i>	Hyperleukocytosis	ND	Matched sibling	No
411	48	NK	<i>ASXL1</i> , <i>IDH2</i>	Adverse genetic mutation	Nil	MUD	No
449	48	+8	<i>IDH2</i> , <i>SRSF2</i>	Adverse genetic mutation	Nil	Matched sibling	No
723	58	NK	<i>NPM1</i> , <i>FL3</i> -ITD, <i>ASXL1</i>	Adverse genetic mutation	Not detected	Matched sibling	No
724	46	NK	<i>NPM1</i> , <i>FLT3</i> -ITD, <i>PTPN11</i> , <i>WT1</i>	Adverse genetic mutation	Not detected	Matched sibling	No
744	53	NK	<i>NRAS</i> , <i>MLL</i>	Hyperleukocytosis	Nil	Matched sibling	No
859	45	+20	<i>NPM1</i> , <i>FLT3</i> -ITD	Adverse genetic mutation	Not detected	Matched sibling	No
897	63	NK	<i>IDH2</i>	Delayed CR1	Nil	MMUD	Yes
938	45	NK	<i>NPM1</i> , <i>CEBPA</i> , <i>FLT3</i> -TKD	Hyperleukocytosis	Not detected	Matched sibling	No
942	57	der(21)t(15;21)(q11;p11)	<i>FLT3</i> -ITD	Adverse genetic mutation	Nil	Haploidentical	No
943	45	+21	<i>IDH2</i> , <i>ETV6</i>	Delayed CR1	Nil	Haploidentical	Yes
946	55	NK	<i>NPM1</i> , <i>FLT3</i> -ITD	Adverse genetic mutation	Not detected	Matched sibling	No
982	53	-X	<i>NPM1</i> , <i>PTPN11</i> , <i>TET2</i>	Flow MRD positive	Detected	Haploidentical	No
1017	32	add(2)(q?31),i(3)(p10),del(7)(q22q32)	<i>IDH1</i>	Adverse cytogenetics	Nil	MUD	Yes
1056	45	NK	<i>FLT3</i> -ITD	Adverse genetic mutation	Nil	Matched sibling	Yes
1069	26	NK	<i>NPM1</i> , <i>IDH2</i> , <i>PTPN11</i>	Flow MRD positive	Detected	Matched sibling	Yes
1092	71	+4	<i>FLT3</i> -TKD, <i>TET2</i> , <i>GATA2</i>	AML intermediate risk	Nil	MUD	Yes
1140	45	del(5)(q11q35),add(13)(p12),add(13)(q32),dic(14;19)(p12;q13),-15,del(17)(p11p13),der(20)t(19;20)(q13;p13)	<i>CEBPA</i> , <i>TP53</i>	Adverse cytogenetics and genetic mutations	Nil	Haploidentical	Yes
1170	66	NK	<i>FLT3</i> -TKD, <i>WT1</i>	AML intermediate risk	Nil	Haploidentical	No

1233	52	NK	Nil	MRD positive	Nil	MMUD	Yes
1259	29	NK	<i>NPM1</i> , <i>RAD21</i> , <i>NRAS</i>	Flow MRD positive	Detected	Matched sibling	No
1303	29	NK	Nil	AML intermediate risk	Nil	Matched sibling	Yes
1436	41	NK	<i>NPM1</i>	Flow MRD positive	Detected	Matched sibling	No
1577	73	NK	<i>ASXL1</i> , <i>IDH2</i>	Adverse genetic mutation	Nil	MUD	No
1609	62	NK	<i>NPM1</i> , <i>FLT3-TKD</i>	Extramedullary involvement	Detected	MUD	No
1701	61	NK	<i>NRAS</i> , <i>IDH2</i> , <i>RUNX1</i>	Delayed CR1	Nil	MUD	Yes

Abbreviations: CR, complete remission; HSCT, hematopoietic stem cell transplantation; MRD, measurable residual disease; MUD, matched unrelated donor; MMUD, mismatched unrelated donor; ND, not done; NK, normal karyotype; OS, overall survival; UPN, unique patient number

Supplementary Table 4. Characteristics of 939 *DNMT3A*-mutated AML patients in the validation cohort

Supplementary Table 4 is available in the supplementary files.

Abbreviations: OS, overall survival

Supplementary Table 5. Characteristics of 63 *DNMT3A*^{mut} patients who had experienced relapse

UPN	Age	Cytogenetics	Co-Mutations	Response to 2 nd line	CR1 duration	Transplant status	Relapsed after HSCT	OS from relapse (months)
26	17	NK	<i>NPM1</i> , <i>FLT3-TKD</i> , <i>RAD</i> , <i>SMC3</i>	CR2	15.4	CR2	Yes	10.3
44	37	NK	<i>TET2</i> , <i>NPM1</i>	CR2	7.0			11.2
49	61	NK	<i>NPM1</i> , <i>FLT3-ITD</i> , <i>PTPN11</i> , <i>WT1</i> , <i>TET2</i>	-	12.7			212.1
82	45	NK	<i>NPM1</i> , <i>FLT3-ITD</i>	-	6.8			2.7
107	46	-Y	<i>NPM1</i> , <i>FLT3-ITD</i> , <i>NRAS</i> , <i>SMC1A</i>	CR2	5.4			13.
115	58	NK	<i>NPM1</i> , <i>IDH2</i>	CR2	93.9			14
135	55	NK	<i>NPM1</i> , <i>NRAS</i>	CR2	10.6			187.9
138	47	NK	<i>FLT3-ITD</i>	CR2	5.9	2nd relapse	Yes	5.8
154	38	NK	<i>NPM1</i> , <i>FLT3-ITD</i> , <i>c-CBL</i>	refractory	1.2			149.7
191	22	NK	<i>NPM1</i> , <i>FLT3-ITD</i> , <i>GATA2</i>	refractory	21.9			33.8
215	43	-Y	<i>NPM1</i> , <i>SMC1A</i>	CR2	2.0	1st relapse	No	80.4
237	35	NK	<i>NPM1</i> , <i>FLT3-ITD</i>	CR2	1.2	2nd relapse	No	14.2
273	50	NK	<i>FLT3-ITD</i> , <i>MLL</i>	refractory	0.5			5.1
301	52	NK	<i>IDH2</i> , <i>STAG2</i>	CR2	6.2	CR2	No	5.4
316	61	t(9;22)(q34;q11)	<i>IDH1</i>	refractory	2.9			88.3

341	42	NK	<i>NPM1, FLT3-ITD</i>	CR2	1.2	CR2	Yes	6.6
343	39	NK	<i>NPM1, NRAS, IDH1</i>	CR2	11.1	1st relapse	No	98.2
360	40	NK	<i>NPM1, FLT3-ITD</i>	refractory	3.7			79.2
380	60	t(5;17)(q33;q21)	<i>NPM1, FLT3-TKD</i>	-	5.8			3.7
407	44	NK	<i>NPM1, FLT3-ITD</i>	CR2	1.6	CR2	Yes	23.1
433	51	NK	<i>NPM1, FLT3-ITD</i>	-	3.8			79.8
496	31	NK	<i>NPM1, FLT3-ITD</i>	refractory	8.8	refractory	Yes	2.
500	29	+11p	<i>ASXL1, IDH2</i>	CR2	3.3	1st relapse	Yes	12.8
533	47	NK	<i>FLT3-ITD</i>	refractory	3.9			58.
550	57	NK	<i>FLT3-ITD</i>	refractory	14.2	refractory	No	16.8
568	35	46,XX,t(2;17)(q2 ?3;p1?3)[1]/45,X,-2,-7,der(17)t(2;17),+mar[1]/43,XX,del(1)(q21q42),+9,t(9;13)(p13;p13),add(11)(p12),-17,+8,-21,-22[1]	<i>NRAS, IDH2, TP53</i>	CR2	121.6			9.7
583	55	NK	<i>NPM1, FLT3-TKD, IDH1</i>	CR2	79.8	CR2	No	19.7
662	61	47,XX,del(X)(p2 ?2),+8	<i>FLT3-TKD, STAG2, IDH1</i>	CR2	8.6			2.
717	42	NK	<i>FLT3-TKD, NRAS, IDH2, SETBP1, STAG2</i>	refractory	3.7	refractory	Yes	12.4
721	54	NK	<i>NPM1, FLT3-ITD</i>	refractory	6.8	refractory	Yes	35.1
755	36	NK	<i>NPM1, FLT3-TKD, RUNX1, CEBPA</i>	CR2	5.7			20.4
775	42	NK	<i>NRAS, TET2</i>	CR2	1.4	1st relapse	No	25.7
820	35	NK	<i>NRAS, KIT, IDH2, GATA2</i>	refractory	3.0	refractory	No	10.5
834	64	NK	<i>NPM1, FLT3-ITD, RUNX1</i>	CR2	5.3	1st relapse	Yes	10.5
838	40	NK	<i>FLT3-ITD, MLL, WT1</i>	refractory	7.2	refractory	Yes	4.6
839	42	NK	<i>IDH2, SMC1A</i>	refractory	1.2	refractory	Yes	14.5
893	50	NK	<i>ASXL1, IDH2</i>	refractory	18.0	refractory	Yes	10.5
896	82	NK	<i>NPM1</i>	CR2	6.1			23.1
918	34	NK	<i>NPM1, IDH2</i>	CR2	18.6	CR3	No	79.8
943	45	47,XY,+21	<i>IDH2, ETV6</i>	CR2	32.3	CR2	Yes	2.0
964	61	NK	<i>NPM1, FLT3-TKD, IDH1</i>	refractory	1.0			4.3

1001	66	NK	<i>NPM1</i> , <i>WT1</i> , <i>CEBPA</i> ,	refractory	8.0			2.8
1017	32	46,XX,add(2)(q?31),i(3)(p10),del(7)(q22q32),inc[cp7]	<i>IDH1</i>	CR2	10.2	CR1	Yes	12.8
1030	62	NK	<i>NPM1</i> , <i>IDH2</i>	refractory	2.5	refractory	Yes	10.3
1037	49	NK	<i>NPM1</i> , <i>FLT3-ITD</i> , <i>PTPN11</i> , <i>NRAS</i> , <i>TET2</i>	CR2	3.7	CR2	Yes	58.3
1043	66	46,XX,inv(11)(p15q23)	<i>WT1</i>	refractory	17.2			2.8
1056	45	NK	-	CR2	12.9	CR1	Yes	16.8
1057	31	NK	<i>NPM1</i> , <i>KRAS</i> , <i>PTPN11</i> ,	CR2	13.0	CR2	No	9.7
1076	53	NK	<i>NPM1</i> , <i>IDH2</i>	CR2	4.2	CR2	No	19.7
1092	71	47,XY,+4	<i>FLT-TKD</i> , <i>TET2</i> , <i>GATA2</i>	-	1.8	CR1	Yes	0.7
1140	45	44,XY,del(5)(q11q35),add(13)(p12),add(13)(q32),dic(14;19)(p12;q13),-15,del(17)(p11p13),der(20)t(19;20)(q13;p13)	<i>TP53</i> , <i>CEBPA</i>	CR2	8.1	CR2	Yes	2.4
1220	37	NK	<i>NPM1</i>	refractory	17.1	refractory	Yes	6.6
1233	52	NK	-	CR2	20.9	refractory	Yes	12.4
1303	67	NK	-	CR2	15.9	CR1	Yes	35.1
1416	64	NK	<i>NPM1</i> , <i>FLT3-ITD</i>	CR2	3.9			20.4
1485	60	46,XY,del(9)(q13q22)	<i>IDH2</i> , <i>SRSF2</i>	-	23.1			0.7
1487	53	NK	<i>NPM1</i> , <i>FLT3-ITD</i> , <i>WT1</i> , <i>RUNX1</i>	refractory	3.5			3.7
1506	59	NK	<i>NPM1</i> , <i>FLT3-ITD</i>	refractory	2.8			5.6
1516	58	NK	<i>NPM1</i> , <i>FLT3-ITD</i>	CR2	10.9	CR2	No	25.7
1570	52	NK	<i>IDH2</i>	refractory	2.0	refractory	Yes	14.0
1607	64	NK	<i>NPM1</i> , <i>PTPN11</i> , <i>IDH1</i>	CR2	4.6	CR2	No	10.5
1701	61	NK	<i>NRAS</i> , <i>IDH2</i>	CR2	6.5	CR1	Yes	10.5
1706	49	NK	<i>NPM1</i> , <i>FLT3-ITD</i>	refractory	1.9	refractory	No	24.7

Abbreviations: CR, complete remission; HSCT, hematopoietic stem cell transplantation; NA, not available; NK, normal karyotype; OS, overall survival; UPN, unique patient number

Supplementary Table 6. Differential expressed genes between *DNMT3A*^{mut} and *DNMT3A*^{wt} AML patients

Supplementary Table 6 is available in the supplementary files.

Supplementary Table 7. Differential expressed genes between *TET2*^{mut} and *TET2*^{wt} AML

within the *DNMT3A*^{mut}/*NPM1*^{mut}/*FLT3*-ITD^{wt} subgroup

Supplementary Table 7 is available in the supplementary files.