Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Patel JP, Gönen M, Figueroa ME, et al. Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. N Engl J Med 2012;366:1079-89. DOI: 10.1056/NEJMoa1112304.

Supplementary Appendix Contents

Statement of Author Contributions……2

Supplementary Methods……2

Supplementary Figure Legends……3

Figure S1……6

Figure S2……20

Figure S3……21

Figure S4……22

Figure S5……23

Figure S6……24

Figure S7……25

Figure S8……26

Figure S9……27

Figure S10……28

Figure S11……29

Table S1……30

Table S2……32

Table S3……38

Table S4……39

Table S5……40

Table S6……41

Table S7……54

Table S8……55

Table S9……56

Table S10……58

Table S11……60

Table S12……61

Table S13……62

Supplementary Appendix

Statement of Author Contributions: JPP, MG, MEF, EP, AF, AM, and RLL designed the study. JPP, MG, OAW, and RLL wrote the manuscript with assistance from AM, MT, and AF. MG and ZS performed statistical analysis of the data. HF, REG, ML, HML, JMR, SL, and MST enrolled patients to the original E1900 trial, provided clinical annotation and provided assistance with analysis and interpretation of the molecular and clinical data. JR, AC, GV, RRH, RPK, and EP performed cytogenetic, flow cytometric, and molecular annotation of samples prior to DNA sequencing. JPP, PVV, ID, ST, MVDB, OA, KH, JC, AV, NDS, AH, and OAW helped to perform DNA sequencing and sequencing analysis.

Supplementary Methods

Diagnostic Samples from ECOG 1900 Clinical Trial: DNA was isolated from pretreatment bone marrow samples of 398 patients enrolled in the ECOG E1900 trial; DNA was isolated from mononuclear cells after Ficoll purification. IRB approval was obtained at Weill Cornell Medical College and Memorial Sloan Kettering Cancer Center. All genomic DNA samples were whole genome amplified using Ø29 polymerase. Remission DNA was available from 241 patients who achieved complete remission after induction chemotherapy. Cytogenetic, fluorescent in situ hybridization, and RT-PCR for recurrent cytogenetic lesions was performed as described previously [3] with central review by the ECOG Cytogenetics Committee.

Integrated Mutational Analysis: Mutational analysis of the entire coding regions of *TET2*, *ASXL1*, *DNMT3A, PHF6, WT1*, *TP53*, *EZH2*, *RUNX1*, and *PTEN* and of coding exons of *FLT3*, *HRAS, KRAS, NRAS*, *KIT*, *IDH1,* and *IDH2* with known somatic mutations was performed using PCR amplification and bidirectional Sanger sequencing as previously described.[13] Primer sequences and PCR conditions are provided in **Table S1.** Target regions in individual patient samples were PCR amplified using standard techniques and sequenced using conventional Sanger sequencing, yielding 93.3% of all trimmed reads with an average quality score of 20 or more. All traces were reviewed manually using Mutation Surveyor (SoftGenetics, State College, PA). All variants were validated by repeat PCR amplification and Sanger resequencing of unamplified diagnostic DNA. All mutations which were not previously reported to be either somatic or germline were analyzed in matched remission DNA, when available, to determine somatic status. All patients with variants whose somatic status could not be determined were censored with regard to mutational status for the specific gene.

***NPM1/CEBPA* Next-Generation Sequencing Analysis**: A mononucleotide tract near the canonical frameshift mutations in *NPM1* and the high GC content of the *CEBPA* gene limited our ability to obtain sufficiently high quality Sanger sequence traces for primary mutation calling. We therefore performed pooled amplicon resequencing of *NPM1* and *CEBPA* using the SOLiD 4 system. We performed PCR amplification followed by barcoding (20 pools each with 20 samples) and SOLiD sequencing. The data was processed through the Bioscope pipeline: all variants not present in reference sequence were manually inspected and validated by repeat PCR amplification and Sanger sequencing.

Mutational Cooperativity Matrix: We adapted the Circos graphical algorithm (http://circos.ca/) to visualize co-occuring mutations in AML patients. The arc length corresponds to the proportion of patient with mutations in the first gene and the ribbon corresponds to the percentage of patients with a coincident mutation in the second gene. Pairwise co-occurrence of mutations is denoted only once, beginning with the first gene in the clockwise direction. Since only pairwise mutations are encoded for clarity, the arc length was adjusted to maintain the relative size of the arc and the correct proportion of patients with a single mutant allele is represented by the empty space within each mutational subset.

Statistical Analysis: Mutual exclusivitity of pairs of mutations were evaluated by fourfold contingency tables and Fisher's exact test. The association between mutations and cytogenetic risk classification was tested using the chi-square test. Hierarchical clustering was performed using the Lance-Williams dissimilarity formula and complete linkage. Survival time was measured from date of randomization to date of death for those who died and date of last follow-up for those who were alive at the time of analysis. Survival probabilities were estimated using the Kaplan-Meier method and compared across mutant and wildtype patients using the log-rank test. Multivariate analyses were conducted using the Cox model.

Proportional hazards assumption was checked by testing for a non-zero slope in a regression of the scaled Schoenfeld residuals on functions of time. Many of the statistical analyses conducted in this study use Cox regression which depends critically on the assumption of proportional hazards. Supplemental Table 3 shows the results of the checks which were conducted for each mutation to determine whether the resultant survival curves (one curve for mutant and one curve for wildtype for each mutation) satisfy this assumption. A significant p-value indicates a departure from the proposal hazard assumption. Out of the 27 mutations included in this study, only a single one significantly deviated from proportional hazards (*MLL*-PTD, p=0.04). Considering the possible multiple testing problem, we would have expected 1-2 significances in this table by chance only hence we conclude that it is acceptable to use the Cox regression model for all mutations.

Forward model selection was employed. When necessary, such as the analyses performed in various subsets, results of the univariate analyses were used to select the variables to be included in the forward variable search. Final multivariate models informed the development of novel risk classification rules. All analyses were performed using SAS 9.2 (www.sas.com) and R 2.12 (www.r-project.org).

Supplementary Figure Legends

Figure S1. This figure shows Circos diagrams for each gene.

Figure S2. This figure shows Circos diagrams for all genes and some relevant cytogenetic abnormalities in patients within cytogenetically-defined favorable-risk (Panel A), intermediate-risk (Panel B), and unfavorable-risk (Panel C) subgroups. The percentage of patients in each cytogenetic risk category with ≥2 mutations is displayed in Panel D. The proportion of intermediate risk patients with 2 or more somatic mutations was significantly higher than of patients in the other 2 cytogenetic subgroups

Figure S3. This Circos diagram shows the mutual exclusivity of *IDH1*, *IDH2*, *TET2*, and *WT1*.

Figure S4. Kaplan-Meier estimates of OS according to mutational status: data are shown for OS in the entire cohort according to the mutational status of *PHF6* (Panel A) and *ASXL1* (Panel B).

Figure S5. Kaplan-Meier survival estimates are shown for *IDH2* (Panel A), *IDH2* R140 (Panel B), *IDH1* (Panel C) and the *IDH2* R172 allele (Panel D) in the entire cohort. Panel E shows both *IDH2* alleles while Panel F shows all three *IDH* alleles (p-value represents comparison of all curves). These data show that the *IDH2* R140 allele is the only IDH allele to have prognostic relevance in the entire cohort.

Figure S6. Kaplan-Meier estimates of OS in patients from the test cohort with core-binding factor alterations with mutations in *KIT* versus those wildtype for *KIT*. *KIT* mutations were not associated with a difference in OS when patients with any core-binding factor alteration (i.e. patients with t(8;21), inv(16), or t(16;16)) were studied (A). In contrast, *KIT* mutations were associated with a significant decrease in OS in patients bearing t(8;21) specifically (B). *KIT* mutations were not associated with adverse OS in patients with inv(16) or t(16;16) (C).

Figure S7. Kaplan-Meier survival estimates for *TET2* in cytogenetically-defined intermediate-risk patients in the cohort.

Figure S8. Kaplan-Meier survival estimates for *NPM1*-mutant patients with cytogenetically-defined intermediate-risk in the cohort. Only those with concomitant *IDH* mutations have improved survival.

Figure S9. The risk classification schema for *FLT3*-ITD widltype (A) and mutant (B) intermediate-risk AML shown in Figure 3 is shown here for normal-karyotype patients only.

Figure S10. Mutational prognostic schema predicts outcome regardless of post-remission therapy with no transplantation (A), autologous transplantation (B), and allogeneic transplantation (C) (p-value represents comparison of all curves). Note, curves represent overall risk categories integrating cytogenetic and mutational analysis (as shown in final column in Figure 3A).

Figure S11. Kaplan-Meier estimates of OS in the entire cohort according to *DNMT3A* mutational status (Panel A and B), *MLL* translocation status (Panel C and D) or *NPM1* mutational status in patients receiving high-dose or standard-dose daunorubicin (Panels E and F). OS in patients according to treatment arm is shown in *DNMT3A* mutant (Panel A) and wild-type (Panel B) patients. Panel C shows OS in *MLL* translocated patients receiving high-dose or standard-dose daunorubicin while Panel D shows OS in non-MLL translocated patients depending on daunorubicin dose. OS in patients according to treatment arm is shown in *NPM1* mutant (Panel E) and wild-type (Panel F) patients as well.

Table S1. Baseline characteristics of the samples in the test, validation, and entire cohort from the ECOG E1900 trial.

Table S2. Genomic DNA primer sequences utilized for comprehensive genetic analysis. All primer sequences are displayed with M13F2/M13R2 tags.

Table S3. P-values for the test of proportional hazards for all mutations identified in the test cohort.

Table S4. Mutational frequency of genes sequenced in patients in the overall ECOG E1900 cohort and within each cytogenetic risk group.

Table S5. Co-occurrences of somatic mutations and cytogenetic abnormalities in the test cohort of 398 AML patients with *de novo* AML from the ECOG E1900 trial.

Table S6. Pairwise correlations between all genetic abnormalities.

Table S7. Frequently co-occurring genetic abnormalities.

Table S8. Mutually exclusive genetic abnormalities.

Table S9. Univariate analysis of the effects of mutations in individual genes on overall survival in the ECOG E1900 cohort.

Table S10. Univariate analysis of mutations in individual genes on intermediate-risk group in the ECOG E1900 cohort.

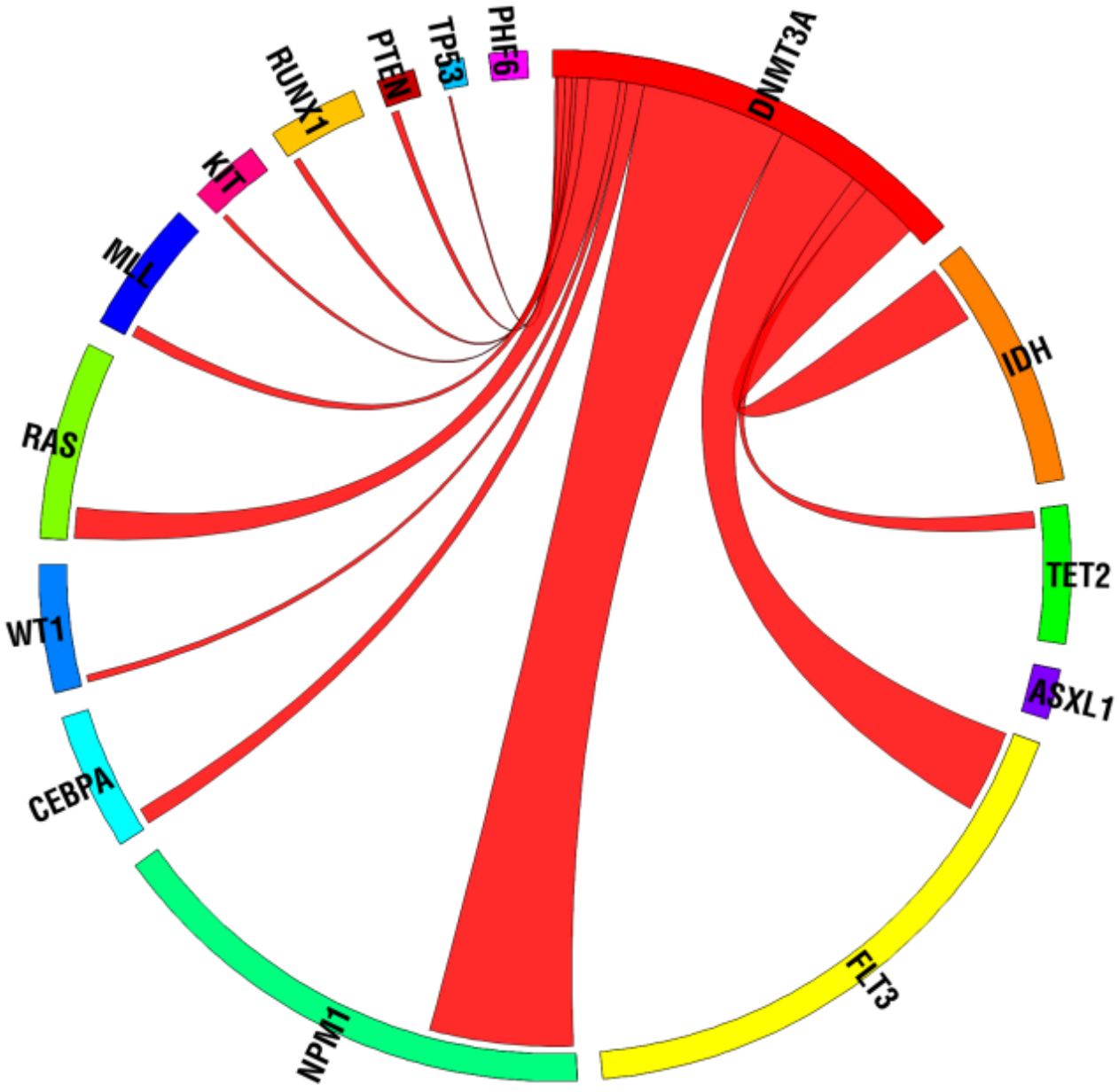
Table S11. Revised AML risk stratification based on integrated genetic analysis with frequency and number of patients in each genetic risk category displayed.

Table S12. Genetic prognostic schema is independent of treatment-related mortality and chemotherapy resistance in the test cohort and the entire cohort of the analyzed ECOG E1900 patients.

Table S13. Differential response to high-dose versus standard-dose daunorubicin induction chemotherapy based on genotype of AML patients.

Figure S1

A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TET2
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MLL
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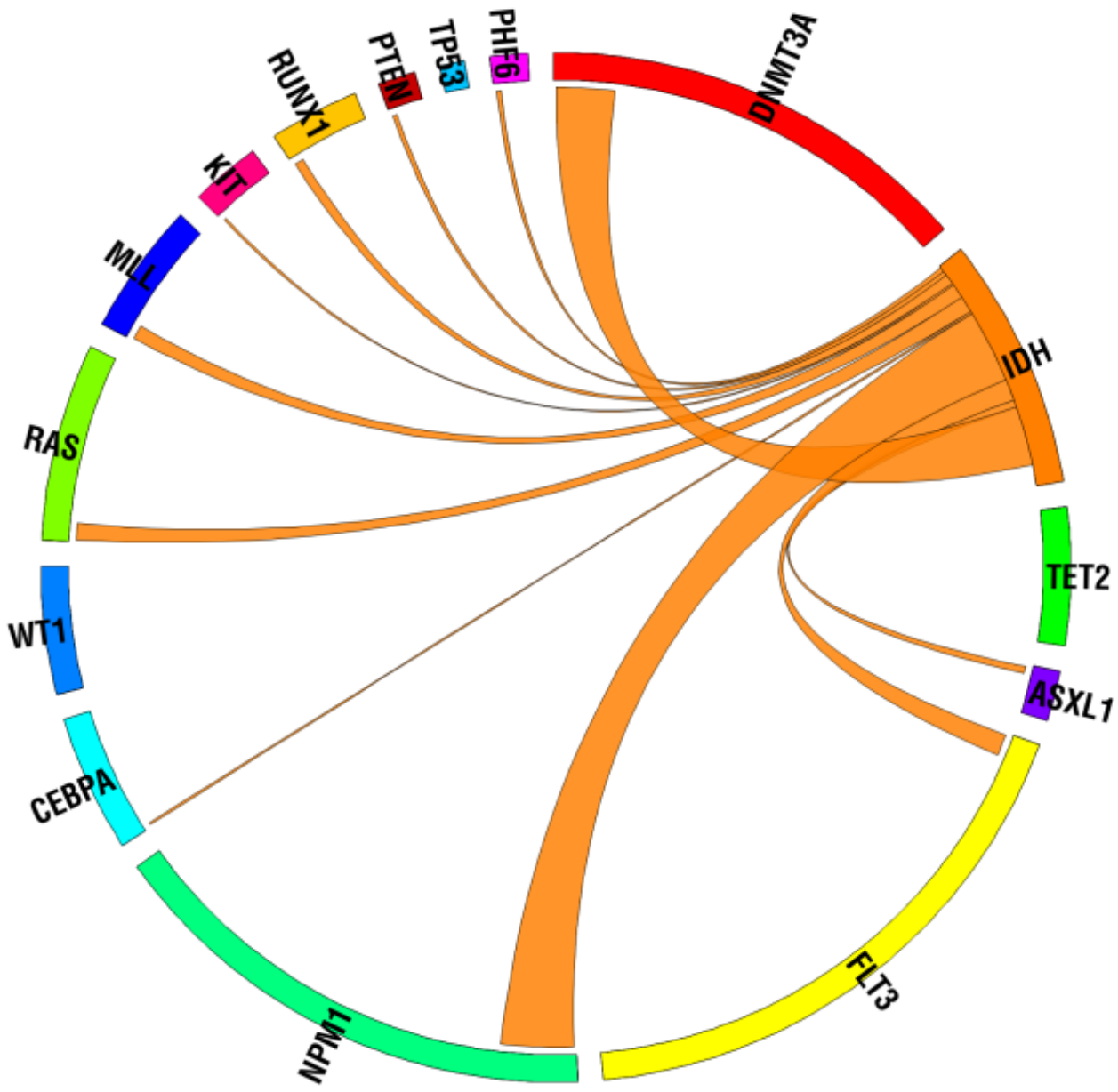
PHF6

Figure S1

B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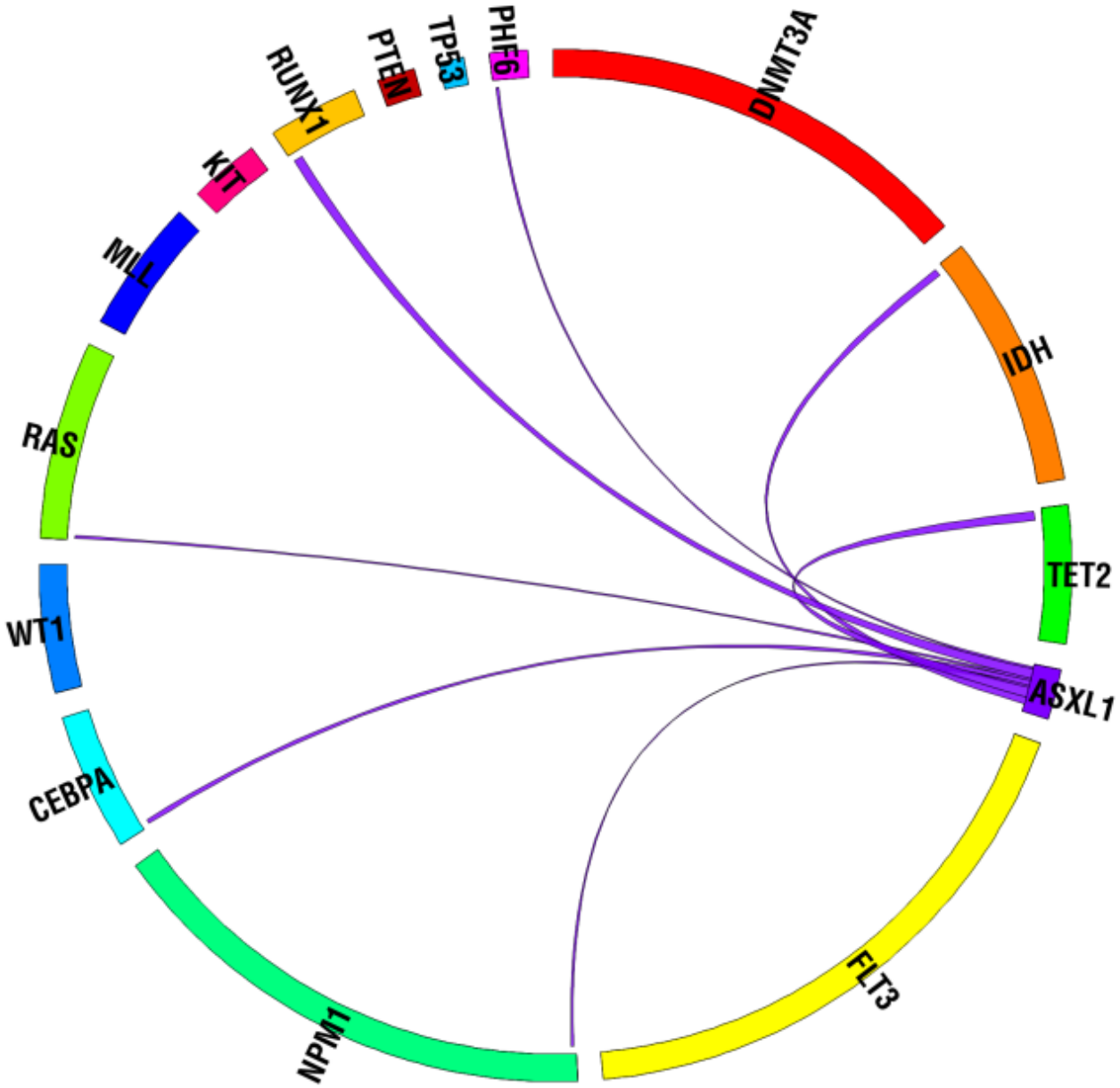
IDH
DNMT3A

Figure S1

C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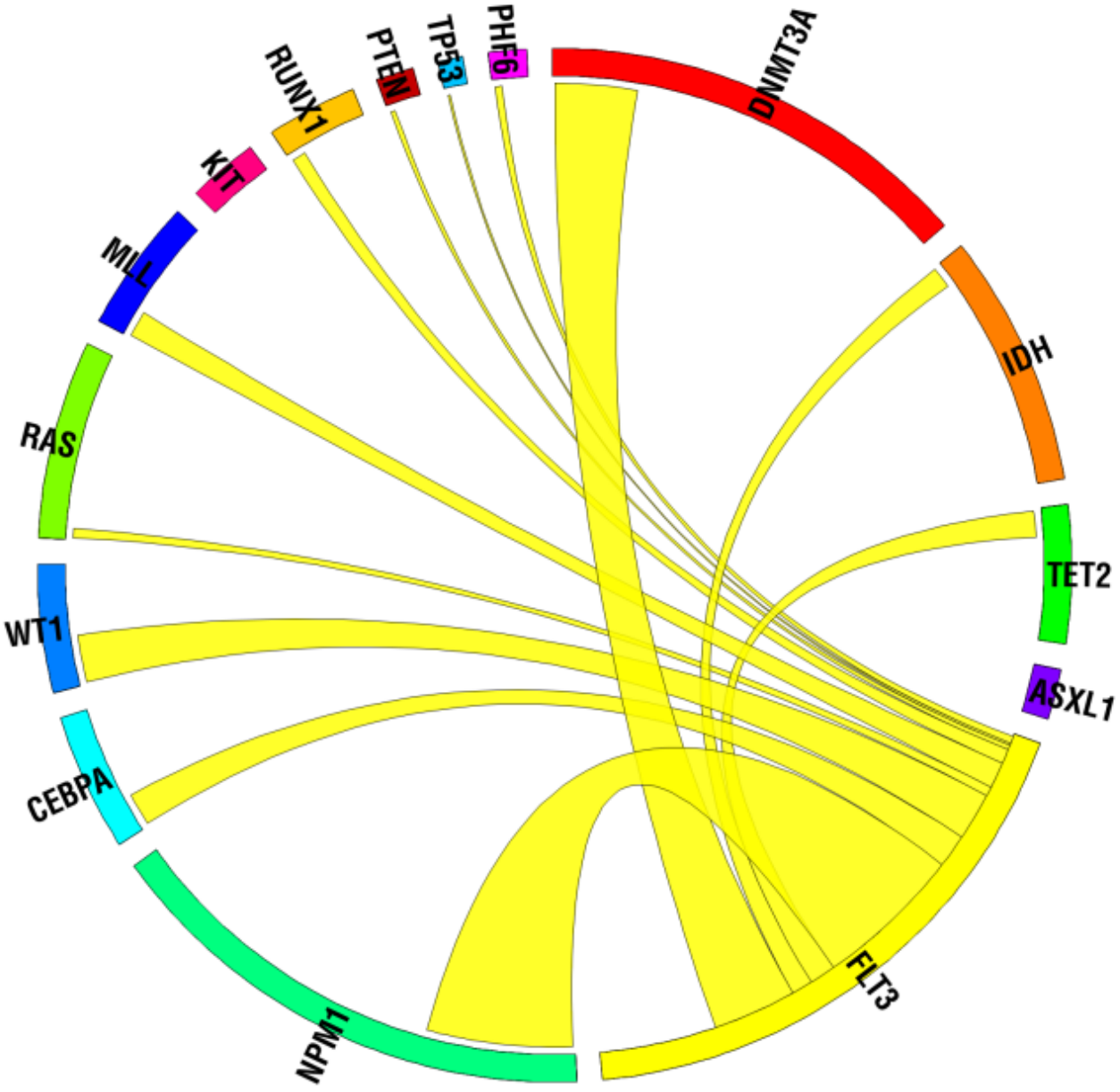
NPM1
FLT3

Figure S1

D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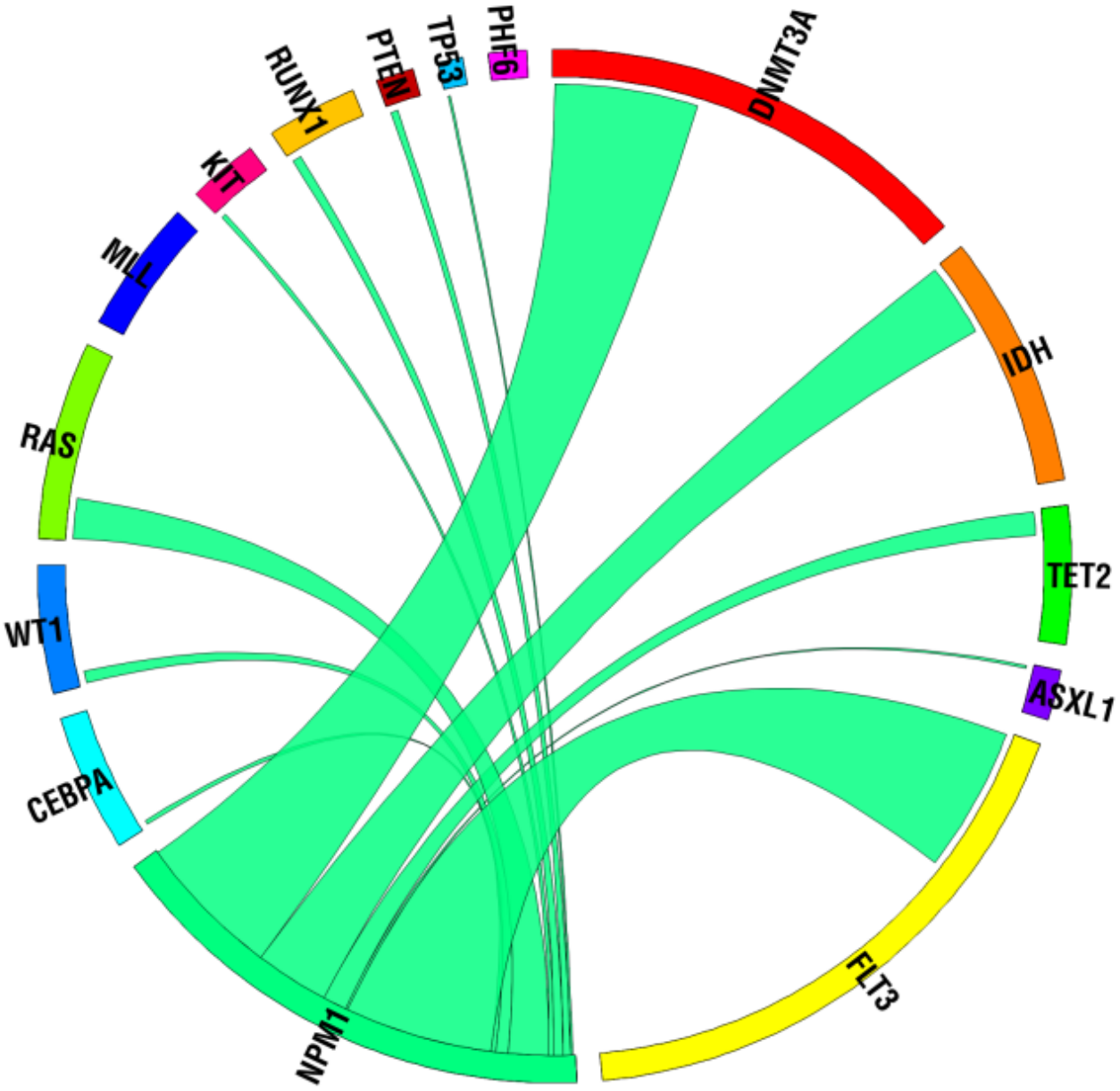
PHF6

Figure S1

E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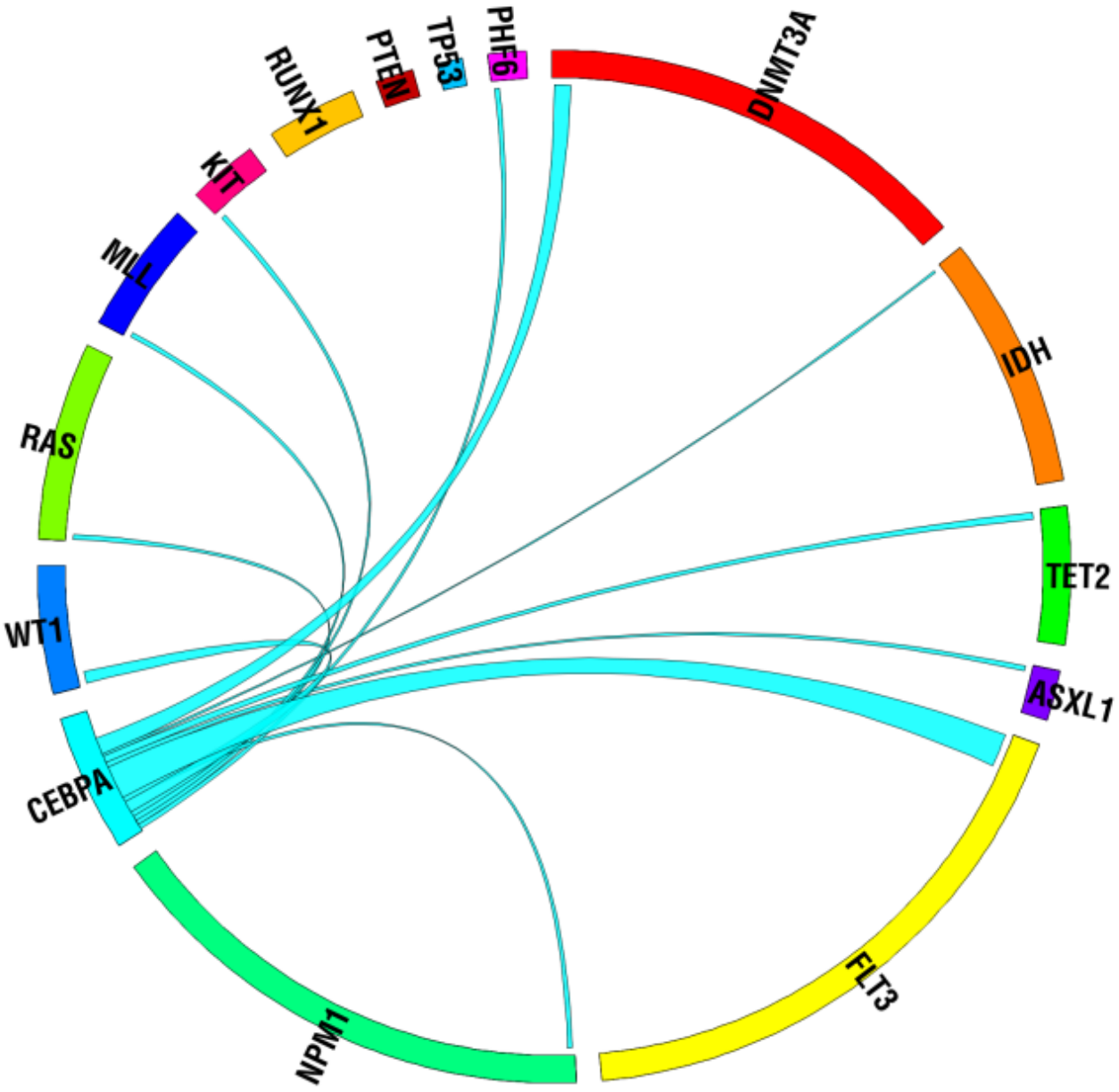
PHF6

Figure S1

F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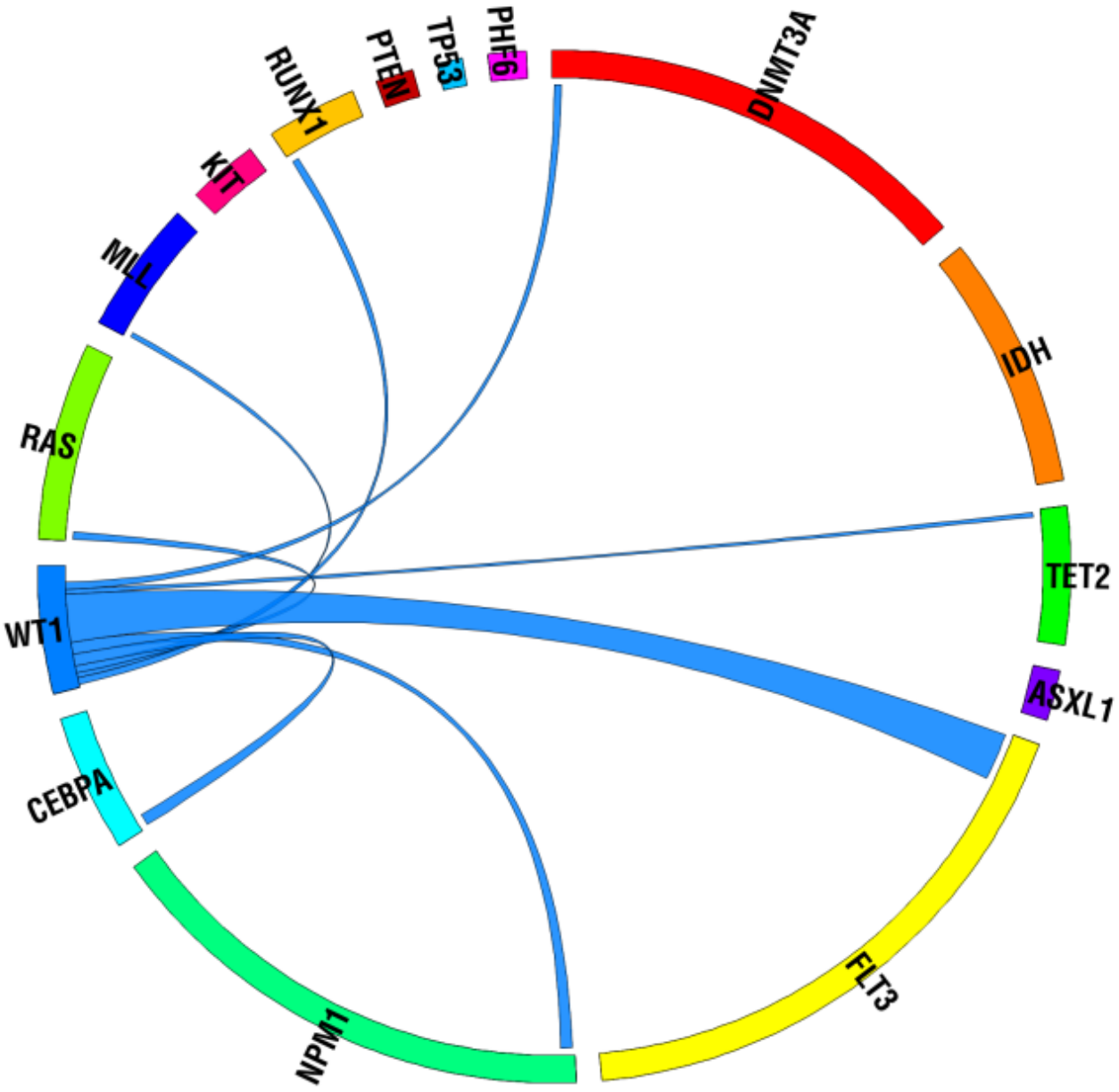
NPM1

Figure S1

G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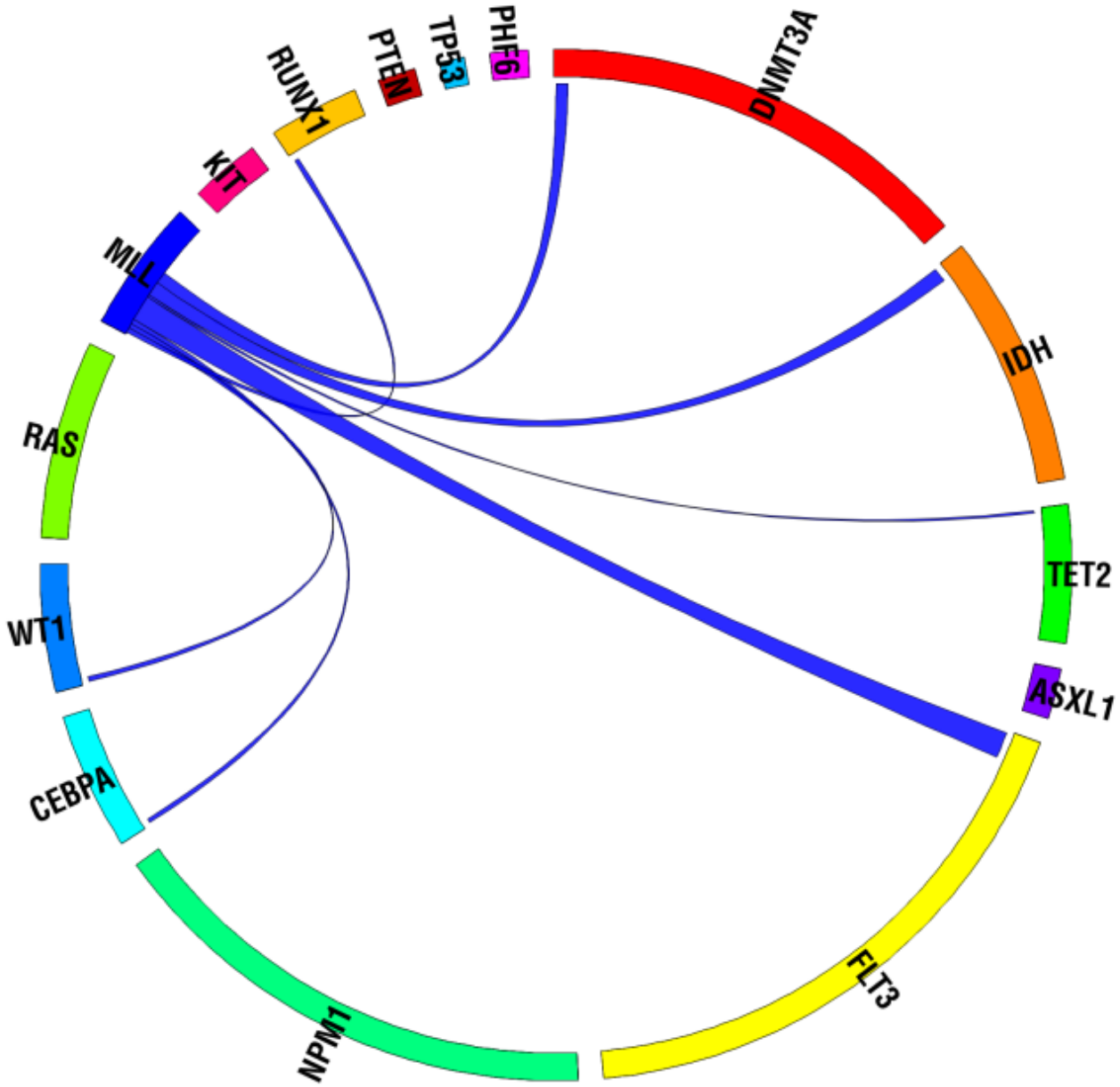
PHF6

Figure S1

H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IDH
DNMT3A

Figure S1

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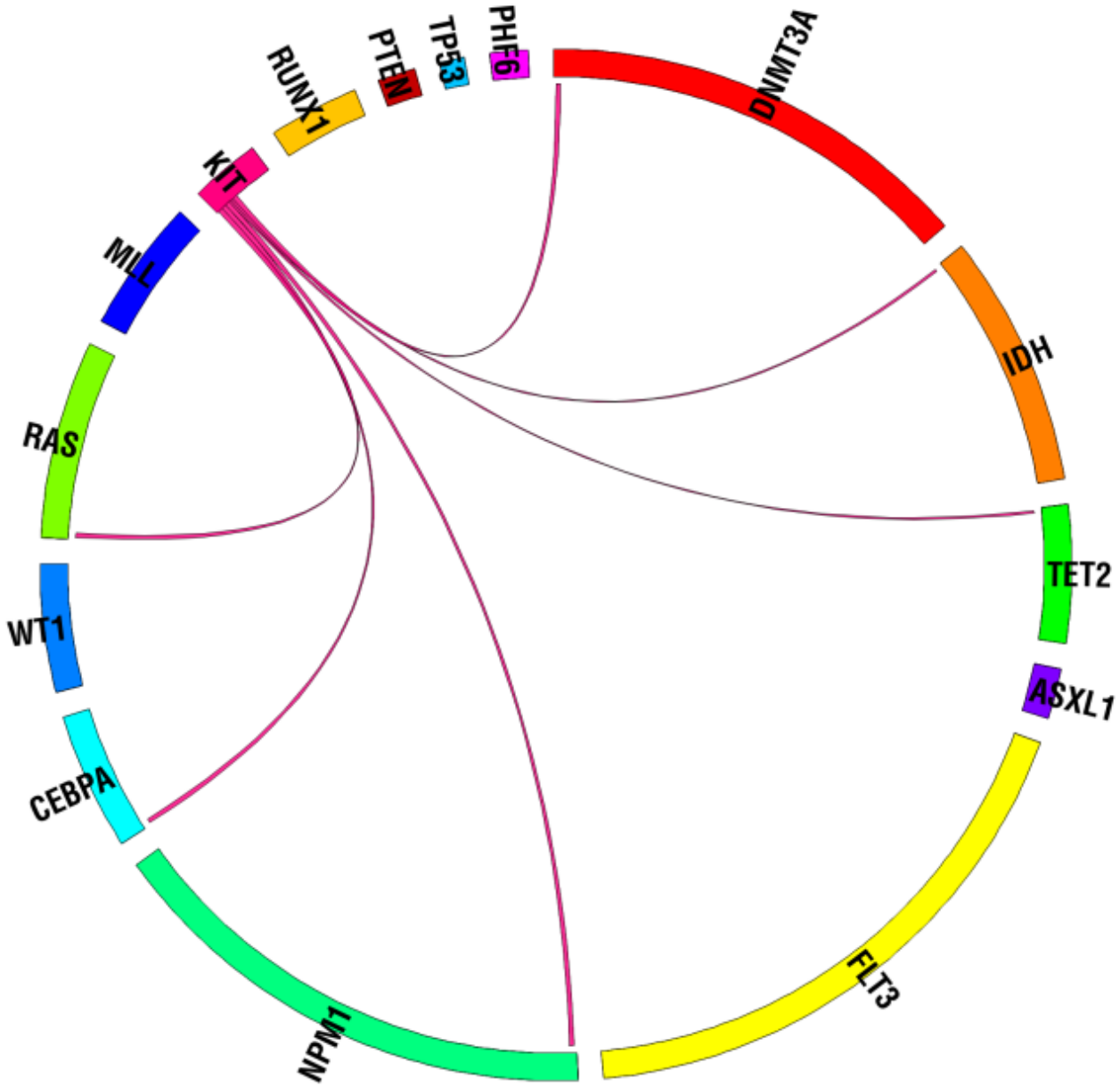
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NPM1

Figure S1

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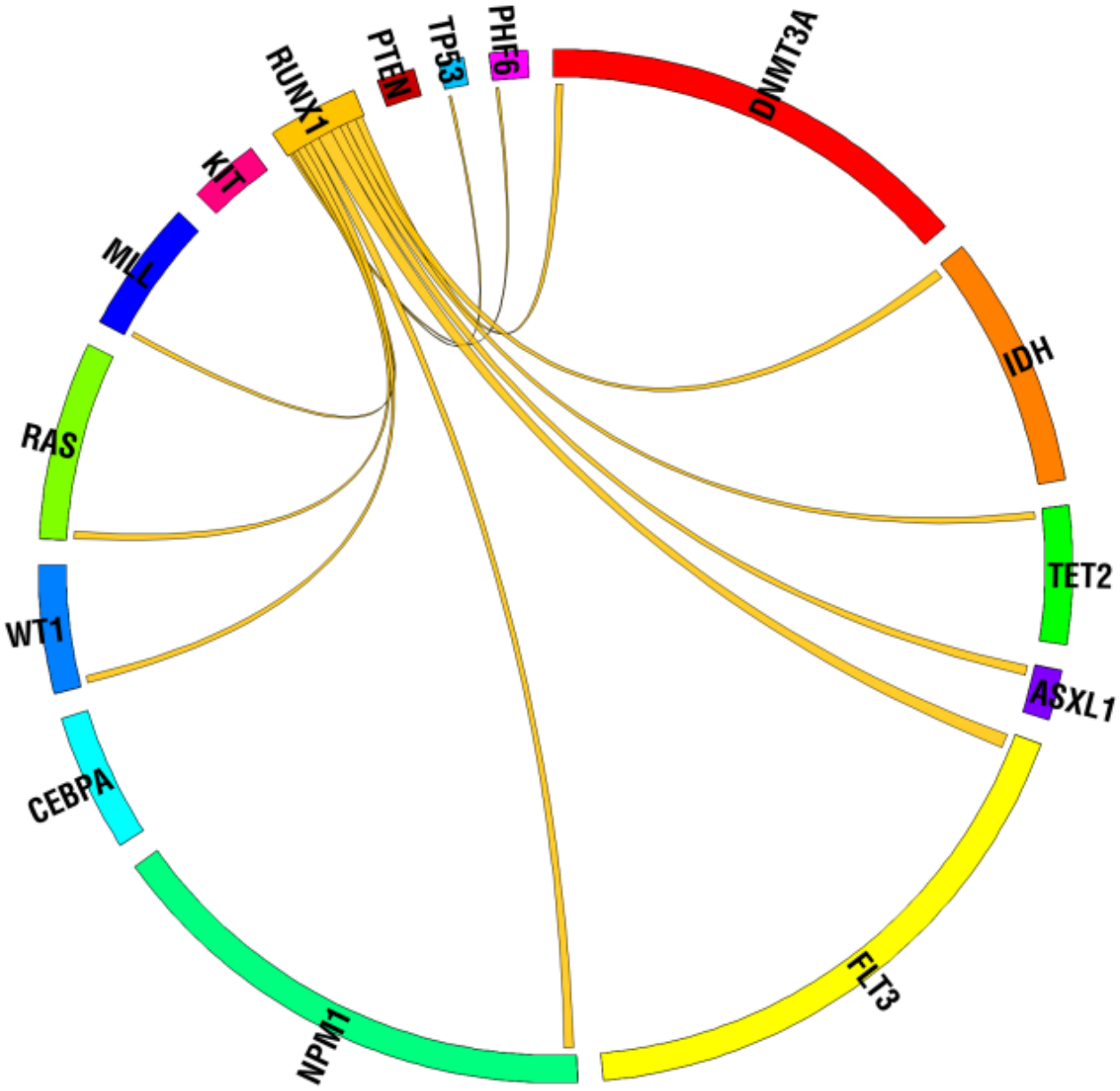
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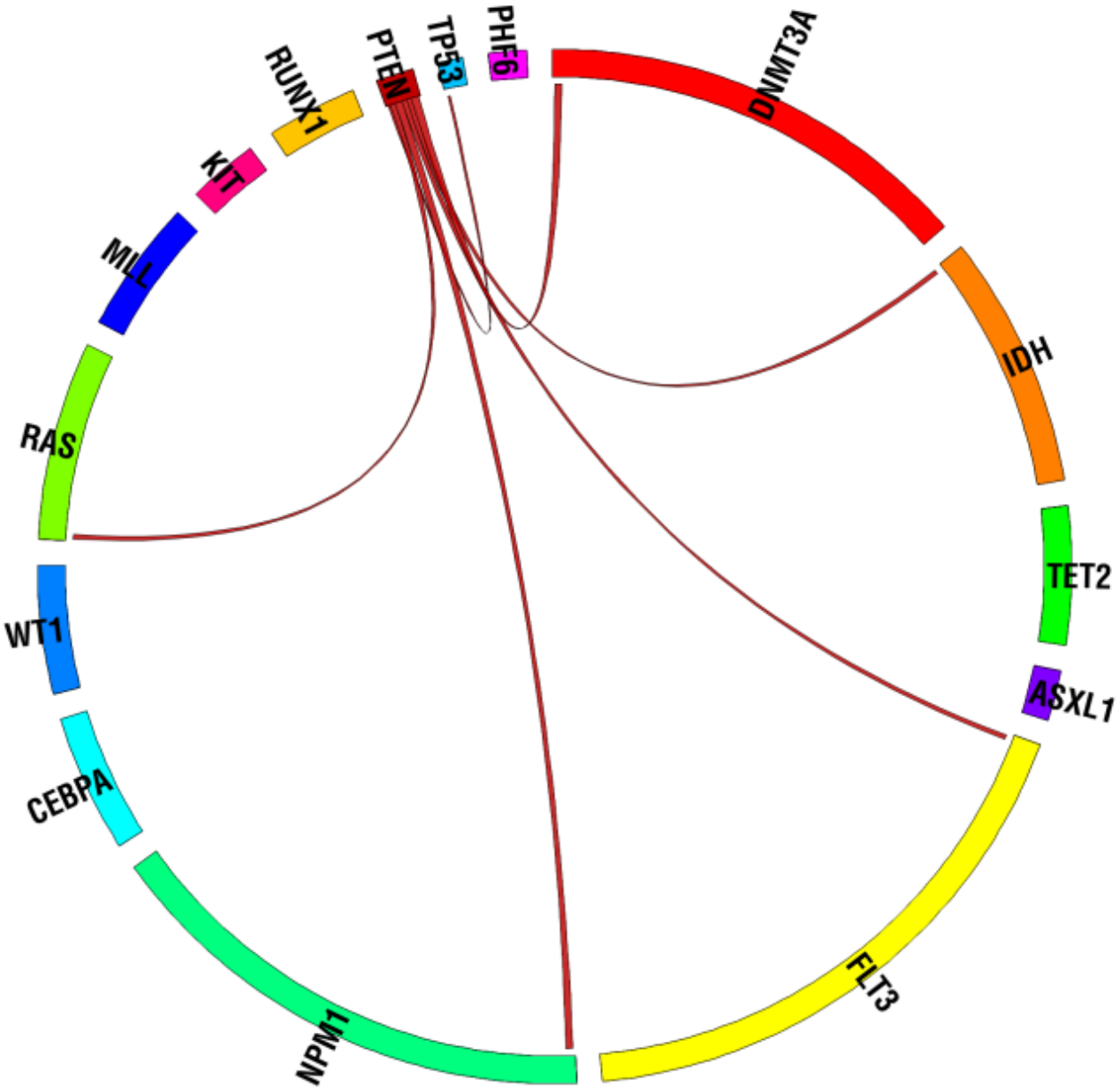
RAS
MLL
KIT

Figure S1

K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PHF6
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FLT3
NPM1

Figure S1

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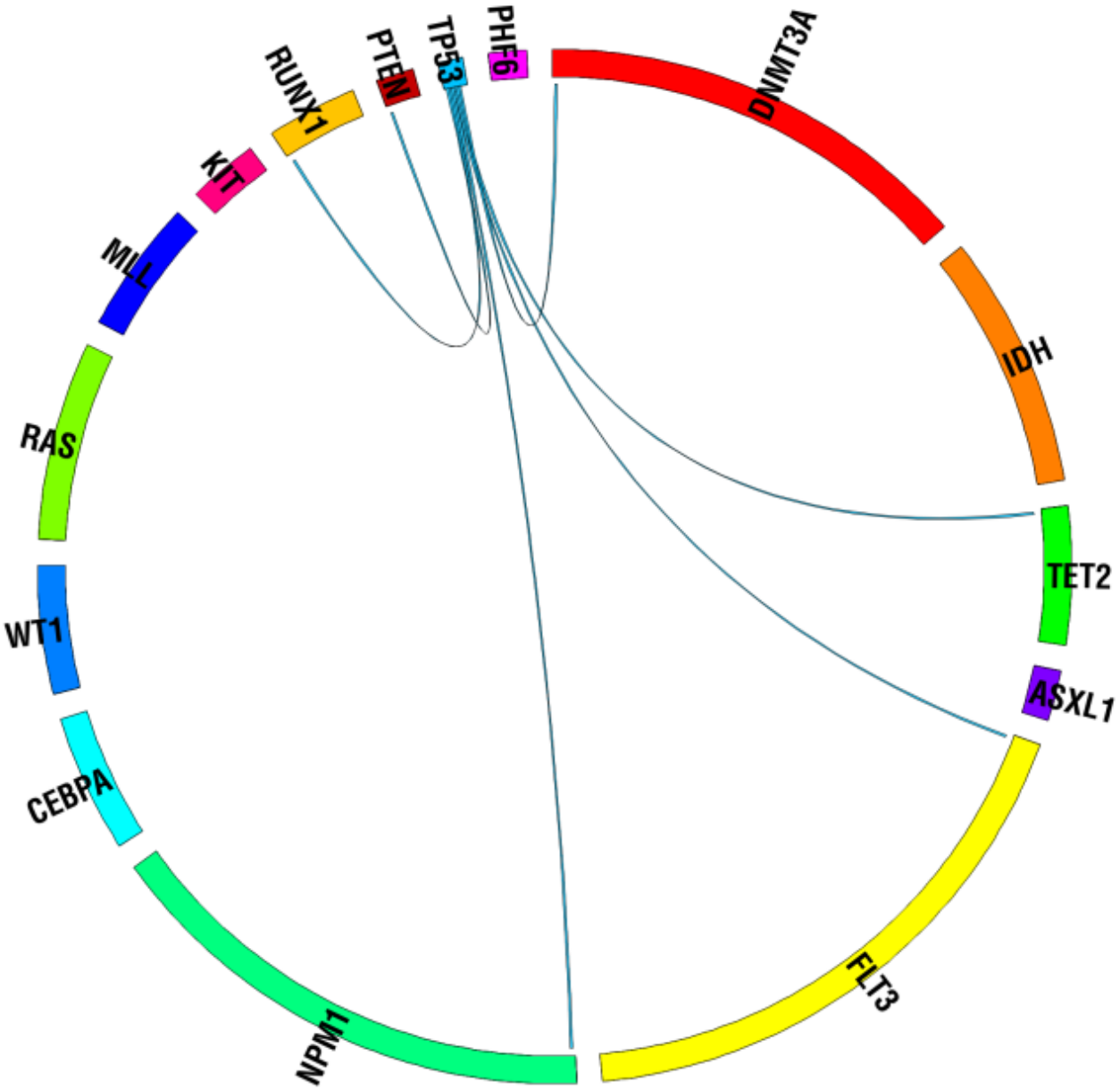
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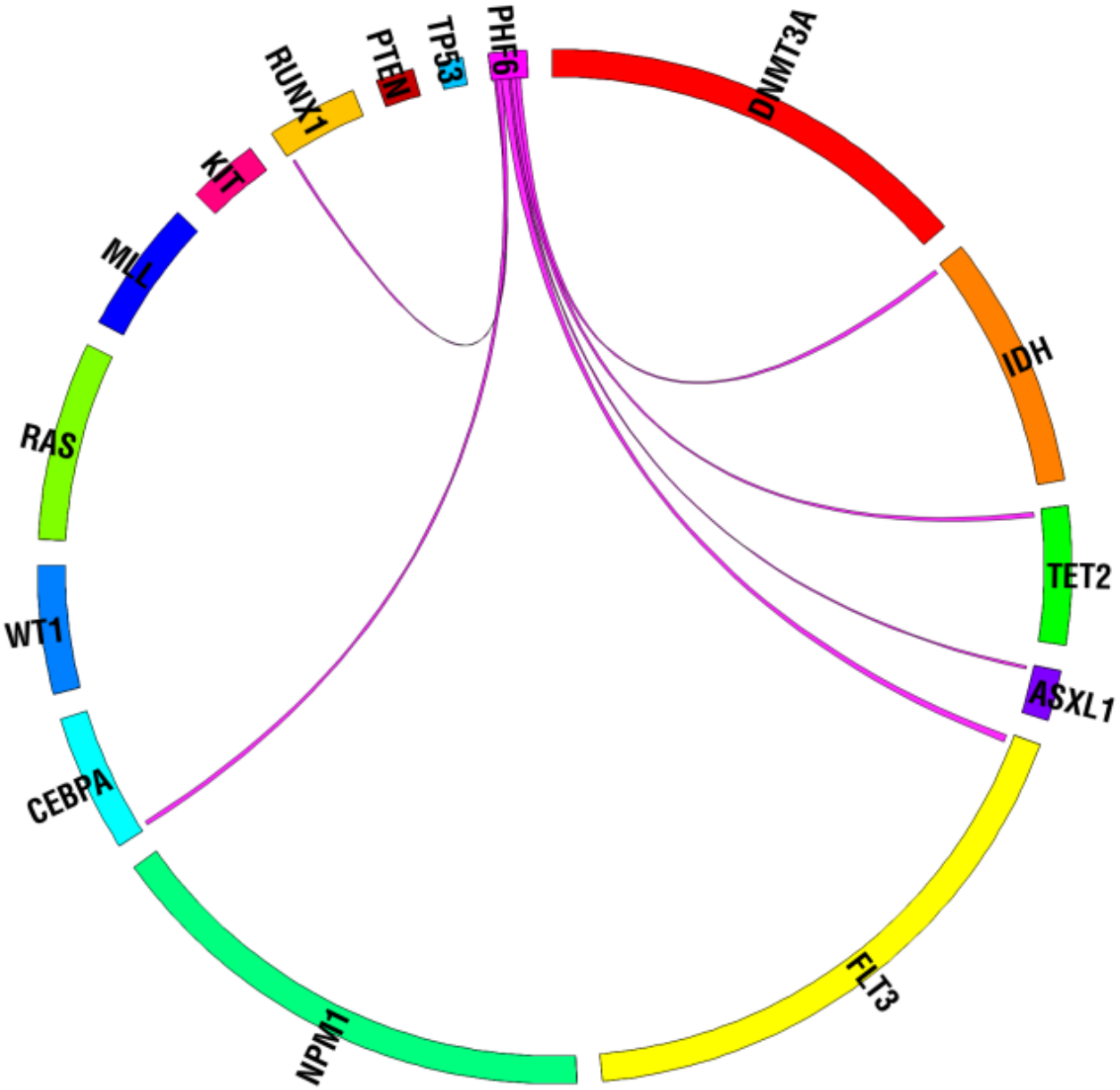
Figure S1

M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TP53

Figure S1

N

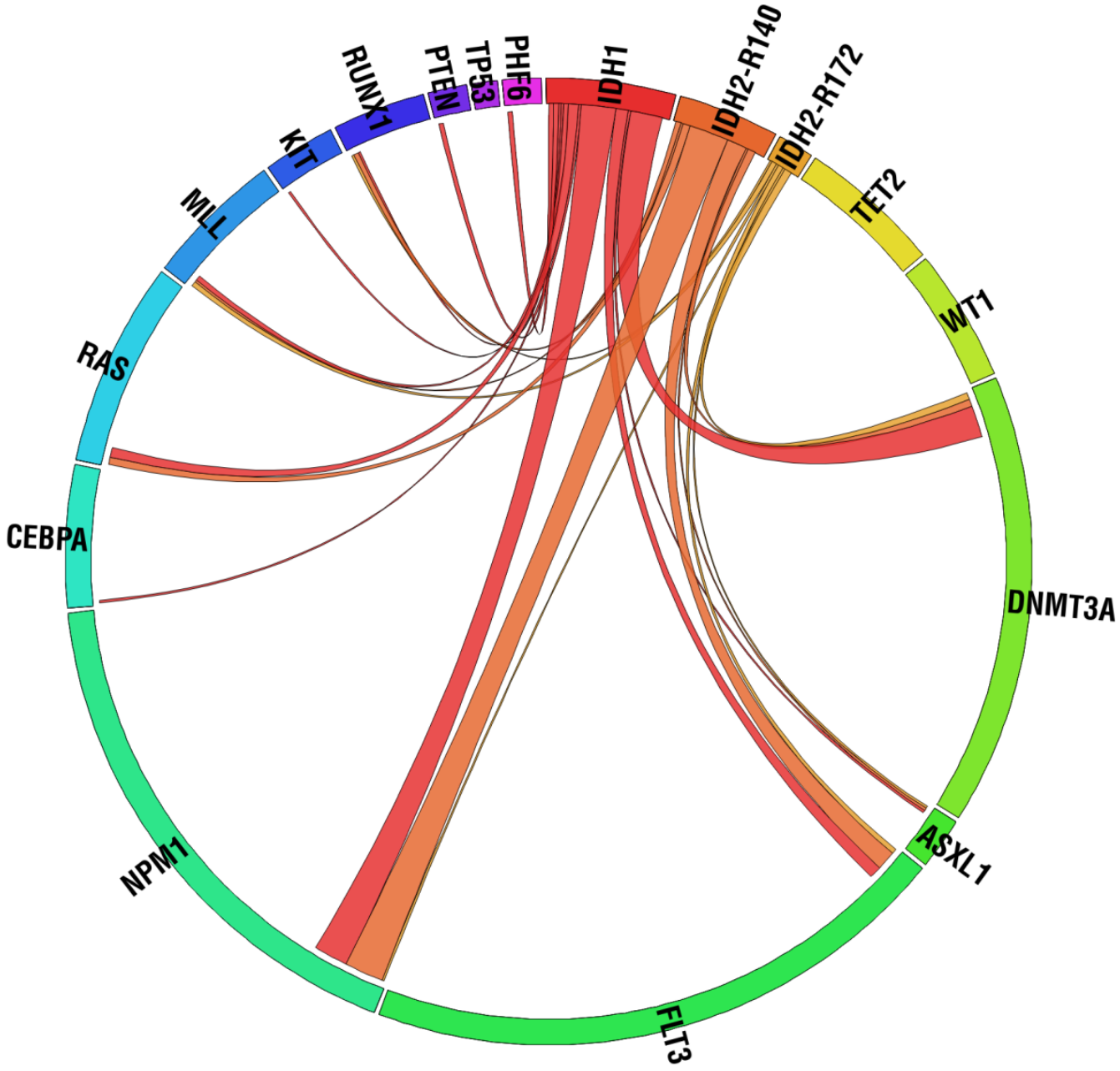
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Figure S2

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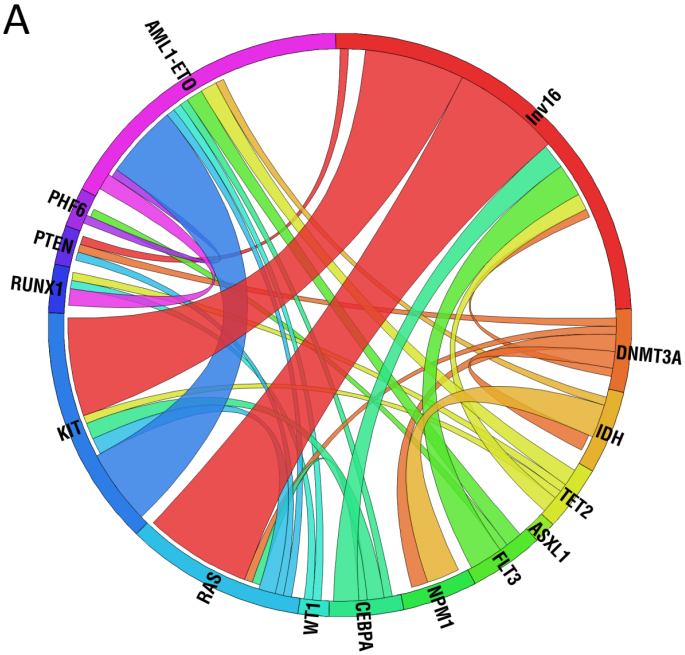

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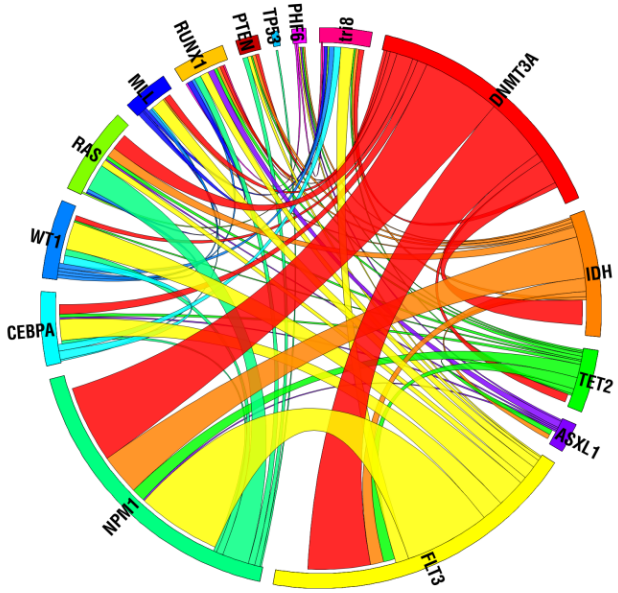

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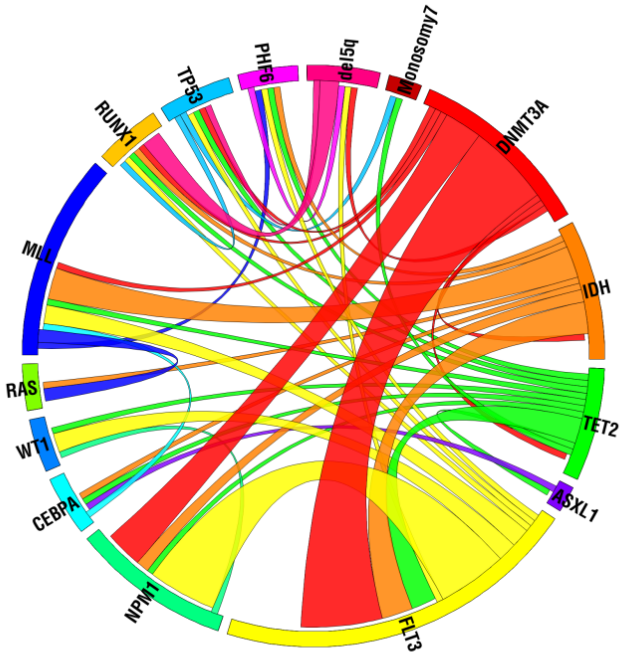
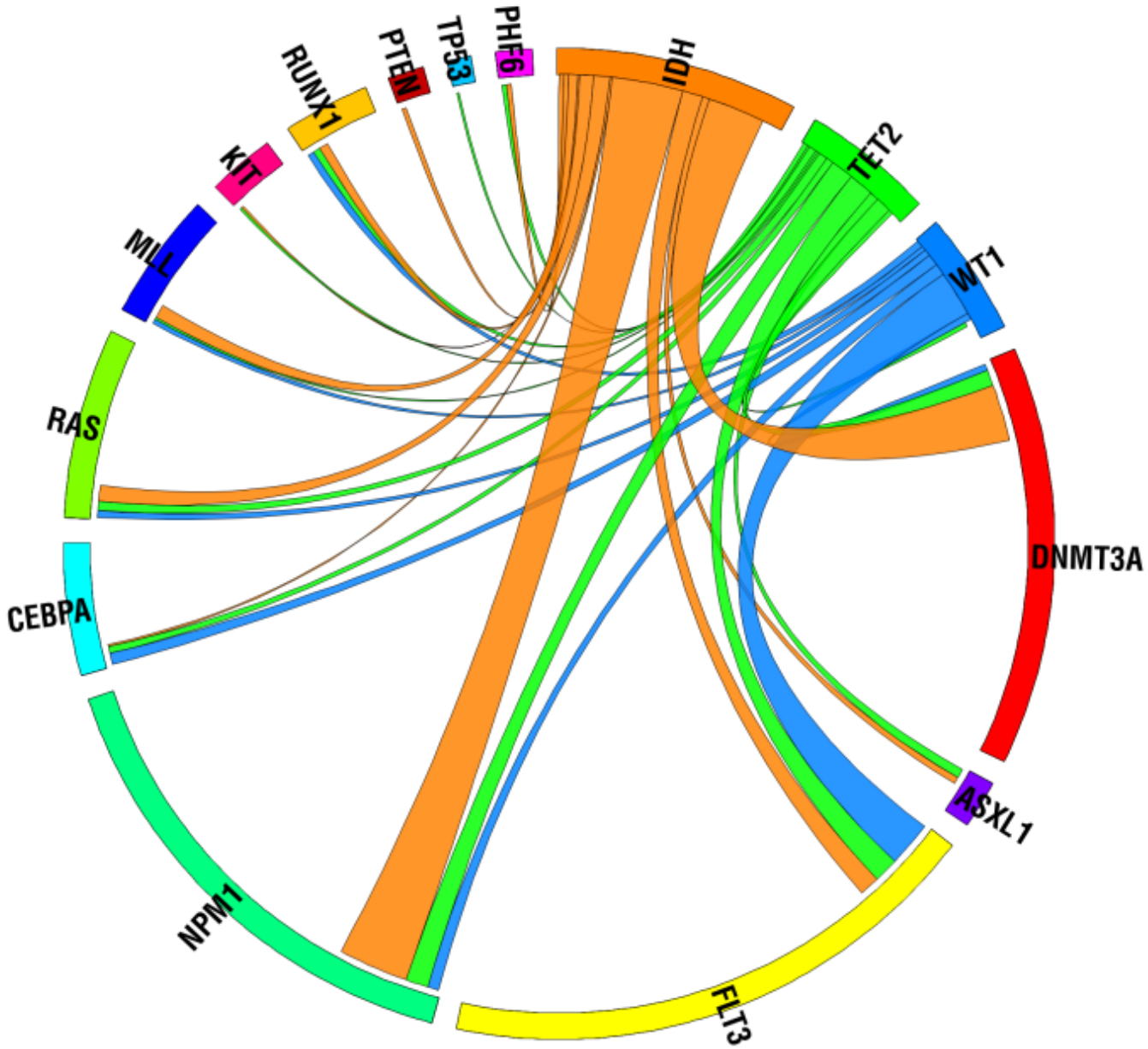


D

Cytogenetic Risk Category	% of samples with ≥ 2 mutations
Favorable	15.5%
Intermediate	69.8%
Unfavorable	24.2%

Figure S3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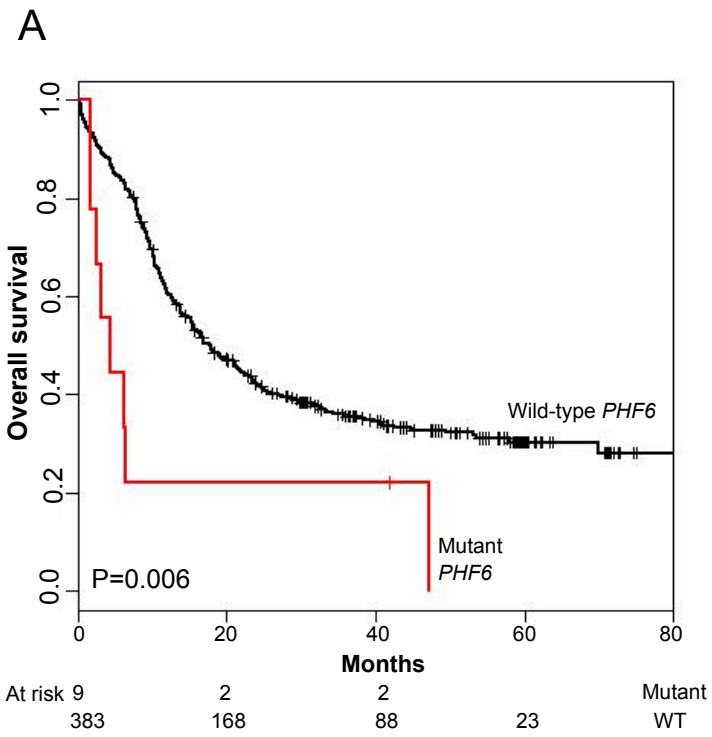
NPM1
FLT3

Figure S4


A
Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
Wild-type PHF6
Mutant
PHF6
P=0.006
0
20
40
60
80
Months
At risk 9 2 2 Mutant
383 168 88 23 WT

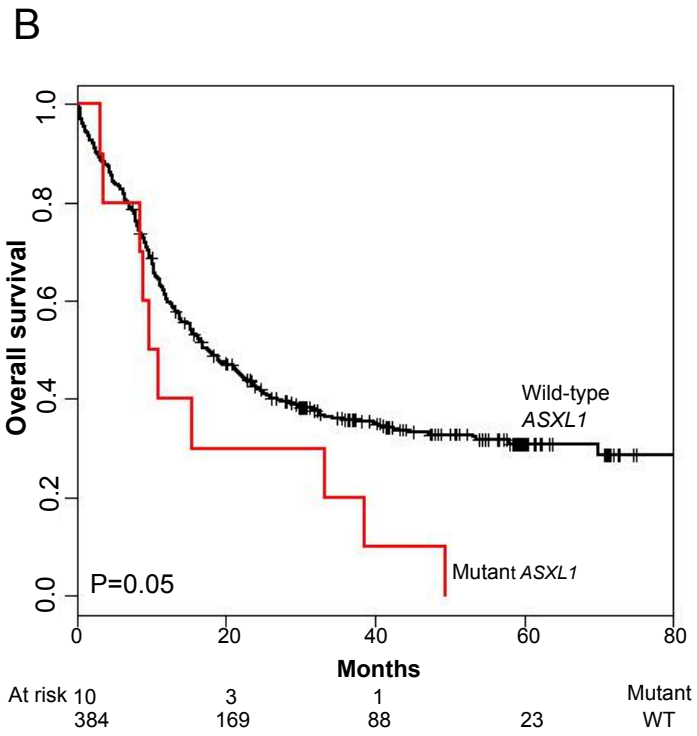

B
Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
Wild-type
ASXL1
Mutant ASXL1
P=0.05
0
20
40
60
80
Months
At risk 10 3 1 Mutant
384 169 88 23 WT

Figure S5

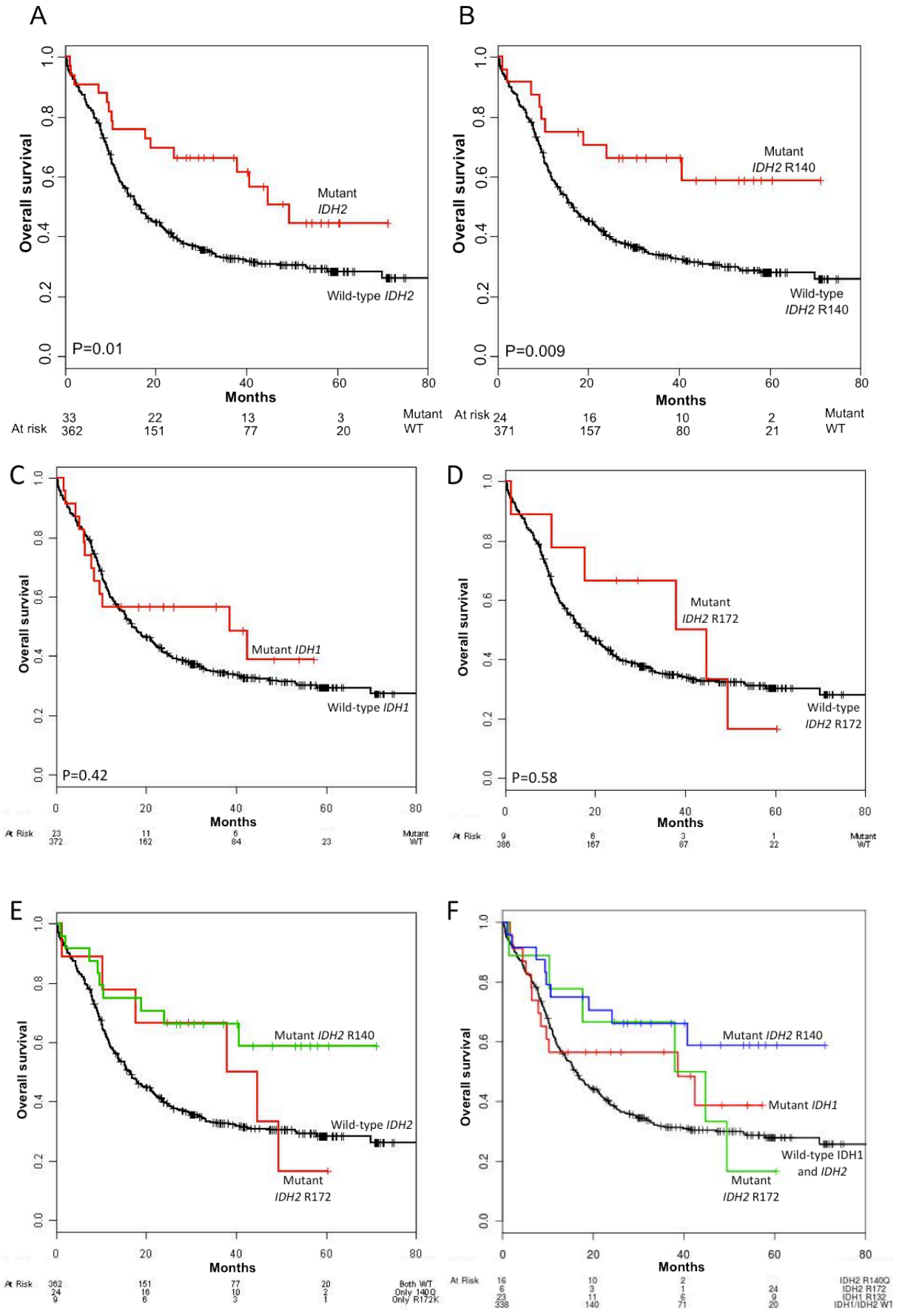
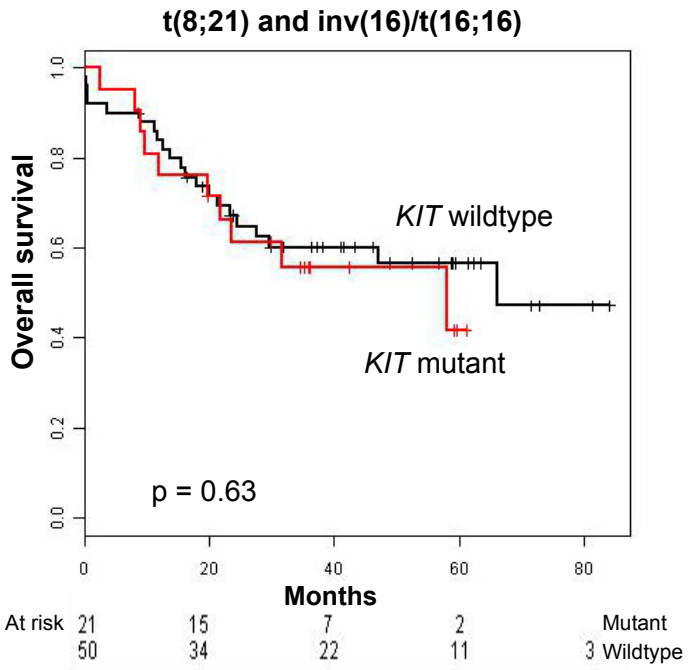
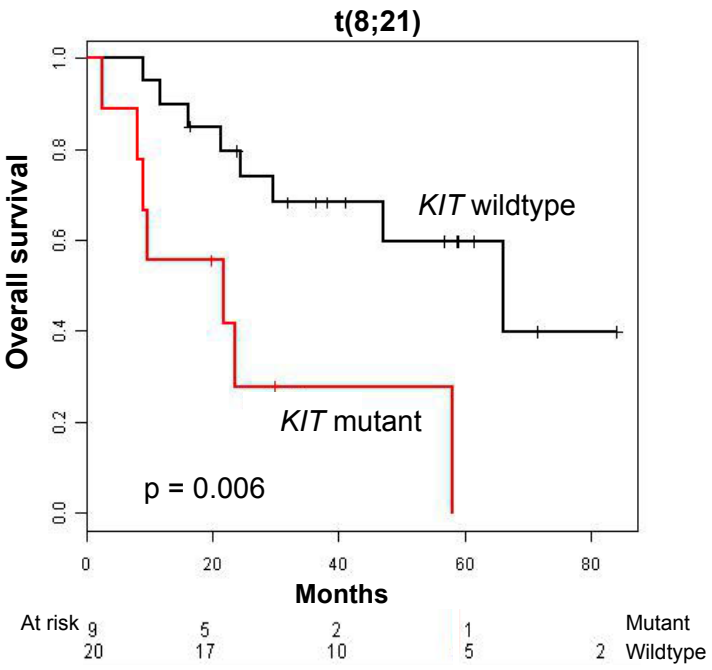

A
Overall survival
Mutant
IDH2
Wild-type IDH2
P=0.01
Months
At risk 33 22 13 3 Mutant
362 151 77 20 WT
B
Overall survival
Mutant
IDH2 R140
Wild-type
IDH2 R140
P=0.009
Months
At risk 24 16 10 2 Mutant
371 157 80 21 WT
C
Overall survival
Mutant IDH1
Wild-type IDH1
P=0.42
Months
At Risk 23 11 6 Mutant
372 162 84 23 WT
D
Overall survival
Mutant
IDH2 R172
Wild-type
IDH2 R172
P=0.58
Months
At Risk 9 6 3 1 Mutant
386 167 87 22 WT
E
Overall survival
Mutant IDH2 R140
Wild-type IDH2
Mutant
IDH2 R172
Months
At Risk 362 151 77 20 Both WT
24 16 10 2 Only 140Q
9 6 3 1 Only R172K
F
Overall survival
Mutant IDH2 R140
Mutant IDH1
Wild-type IDH1
and IDH2
Mutant
IDH2 R172
Months
At Risk 16 10 2 IDH2 R140Q
6 3 1 24 IDH2 R172
23 11 6 9 IDH1 R132
338 140 71 20 IDH1/IDH2 WT

Figure S6


t(8;21) and inv(16)/t(16;16)
Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
KIT wildtype
KIT mutant
p = 0.63
0
20
40
60
80
Months
At risk
21
15
7
2
Mutant
50
34
22
11
3
Wildtype


t(8;21)
Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
KIT wildtype
KIT mutant
p = 0.006
0
20
40
60
80
Months
At risk
9
5
2
1
Mutant
20
17
10
5
2
Wildtype

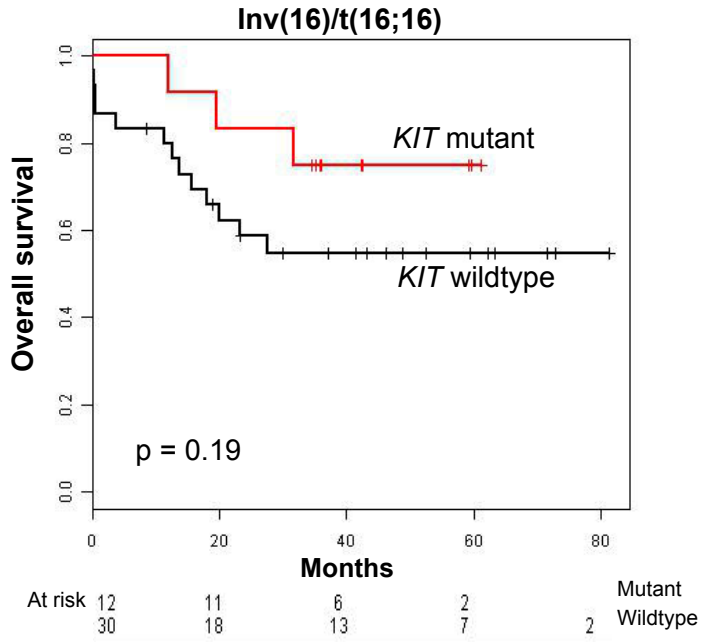

Inv(16)/t(16;16)
Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
KIT mutant
KIT wildtype
p = 0.19
0
20
40
60
80
Months
At risk
12
11
6
2
Mutant
30
18
13
7
2
Wildtype

Figure S7

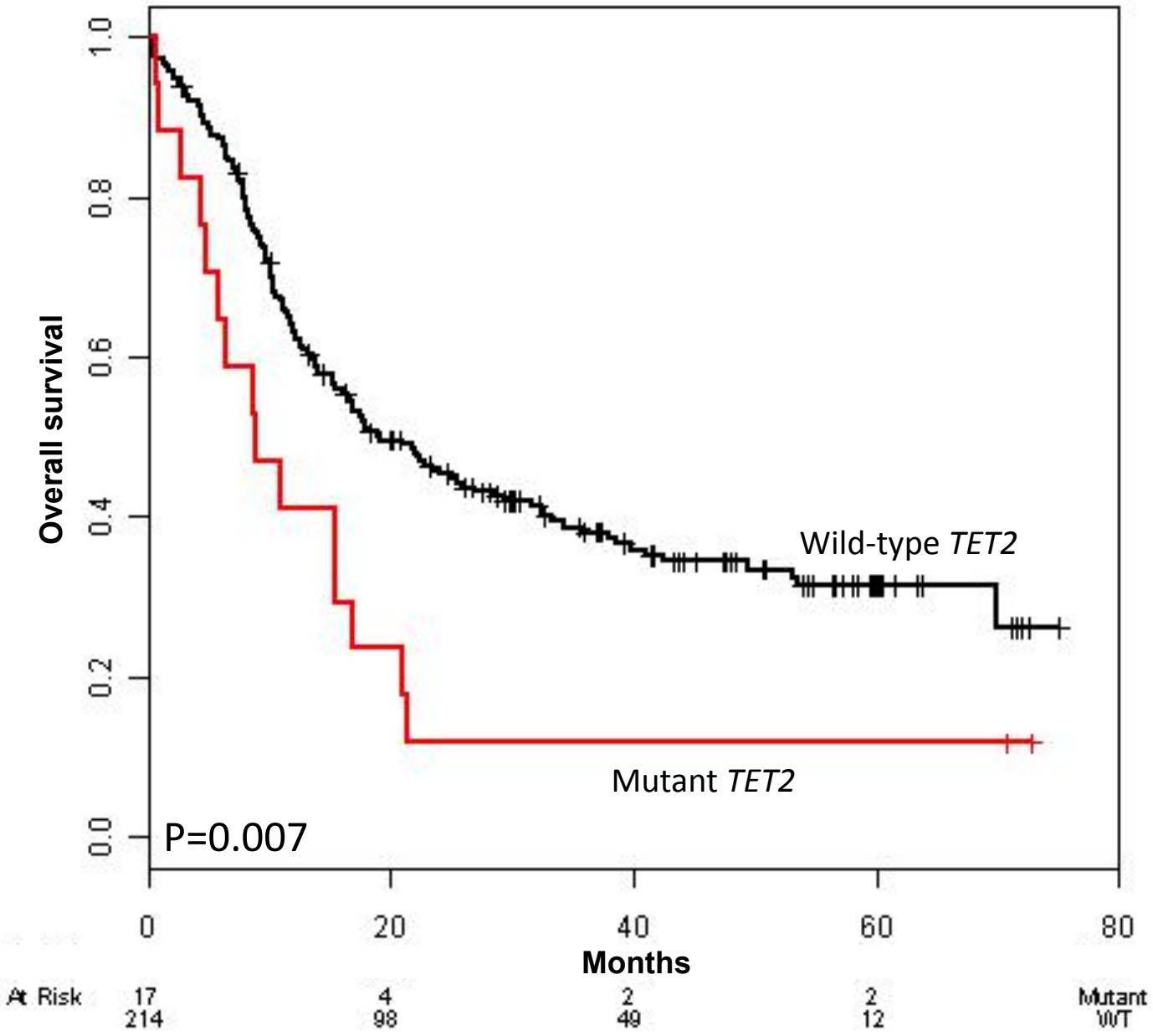

Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
Wild-type *TET2*
Mutant *TET2*
P=0.007
0
20
40
60
80
Months
At Risk
17
214
4
98
2
49
2
12
Mutant
WT

Figure S8

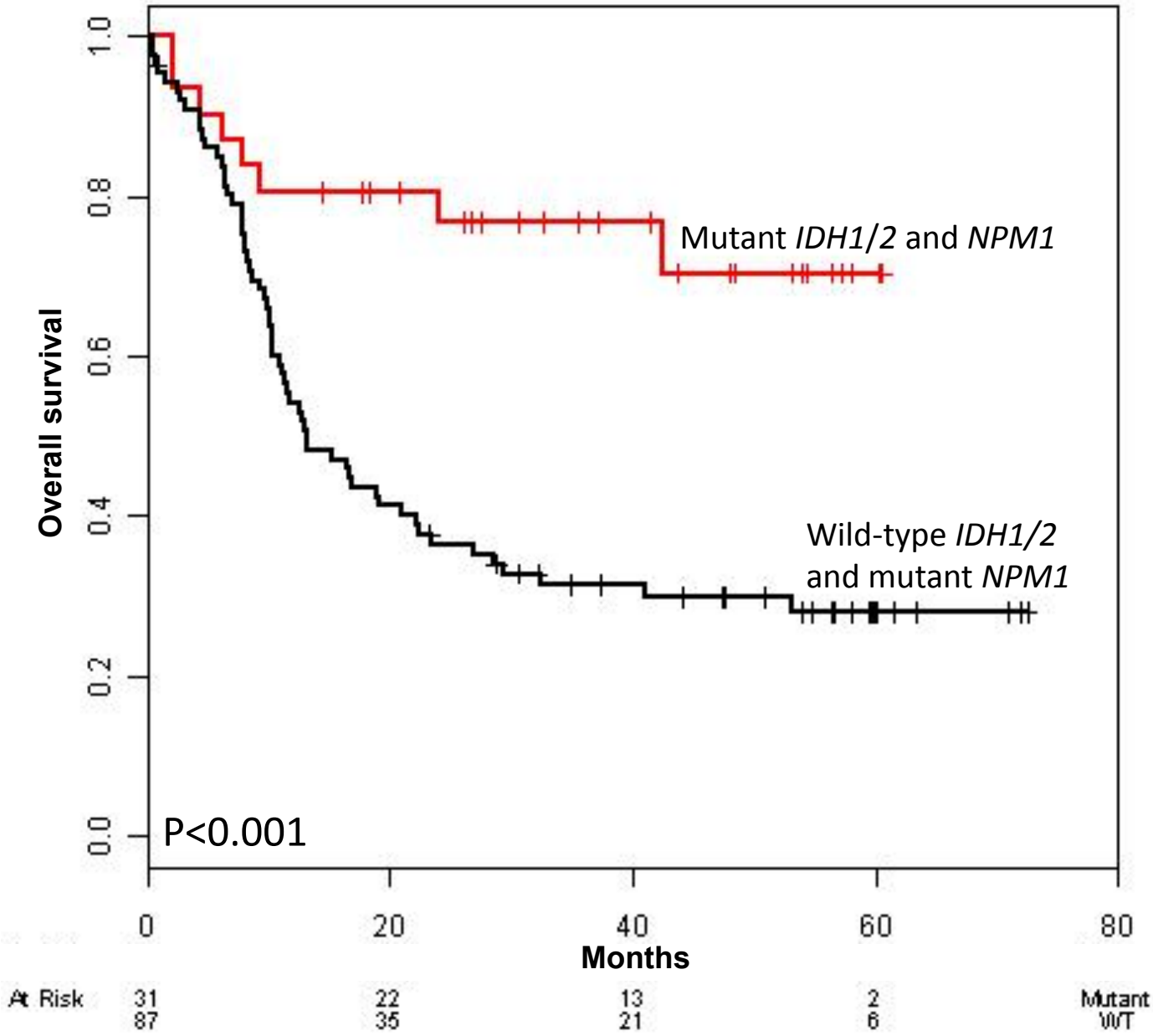
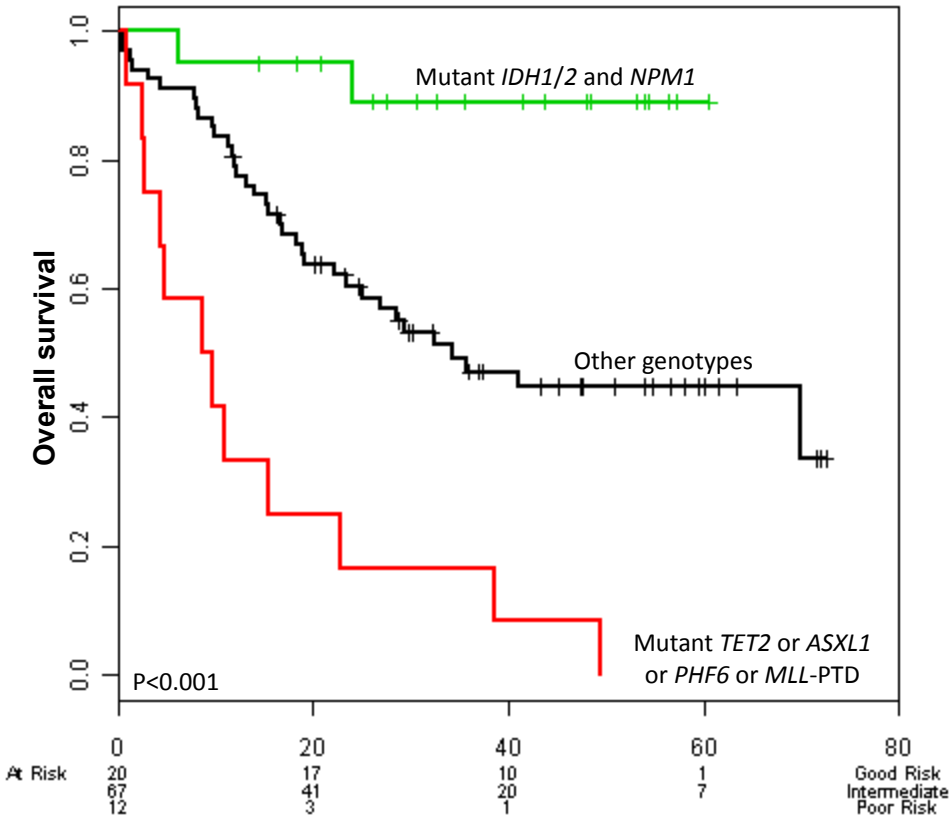

Overall survival
1.0
0.8
0.6
0.4
0.2
0.0
Mutant *IDH1/2* and *NPM1*
Wild-type *IDH1/2*
and mutant *NPM1*
P<0.001
0
20
40
60
80
Months
At Risk
31
87
22
35
13
21
2
6
Mutant
WT

Figure S9

A *FLT3*-ITD Negative, Normal-Karyotype Patients



B *FLT3*-ITD Positive, Normal-Karyotype Patients

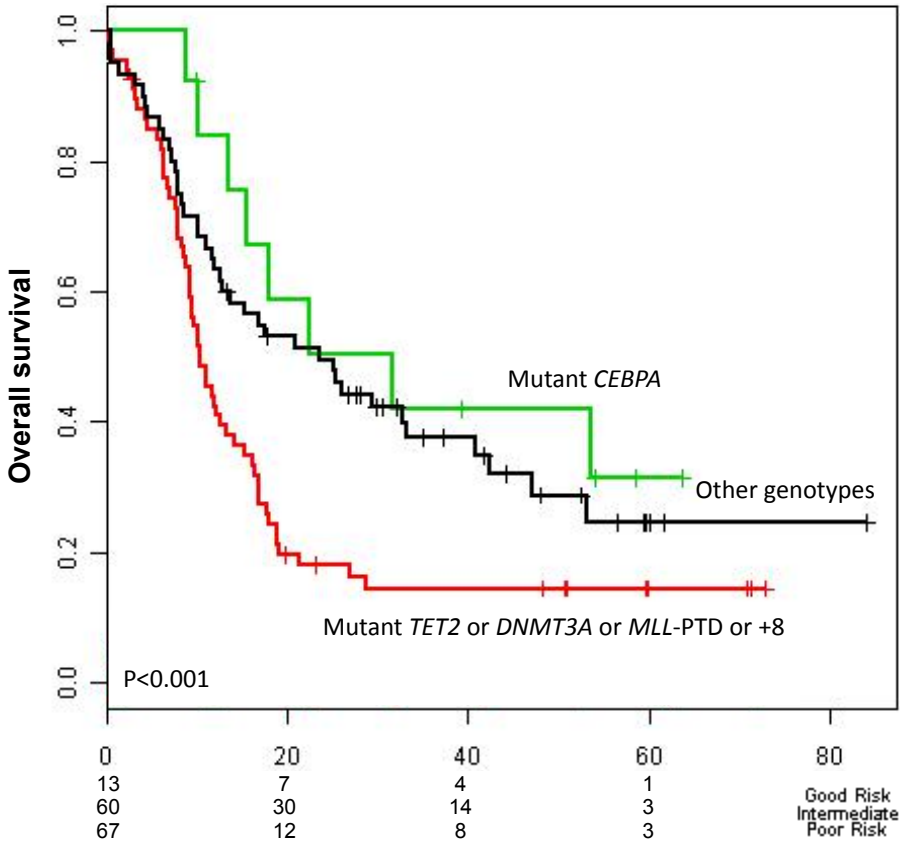


Figure S10

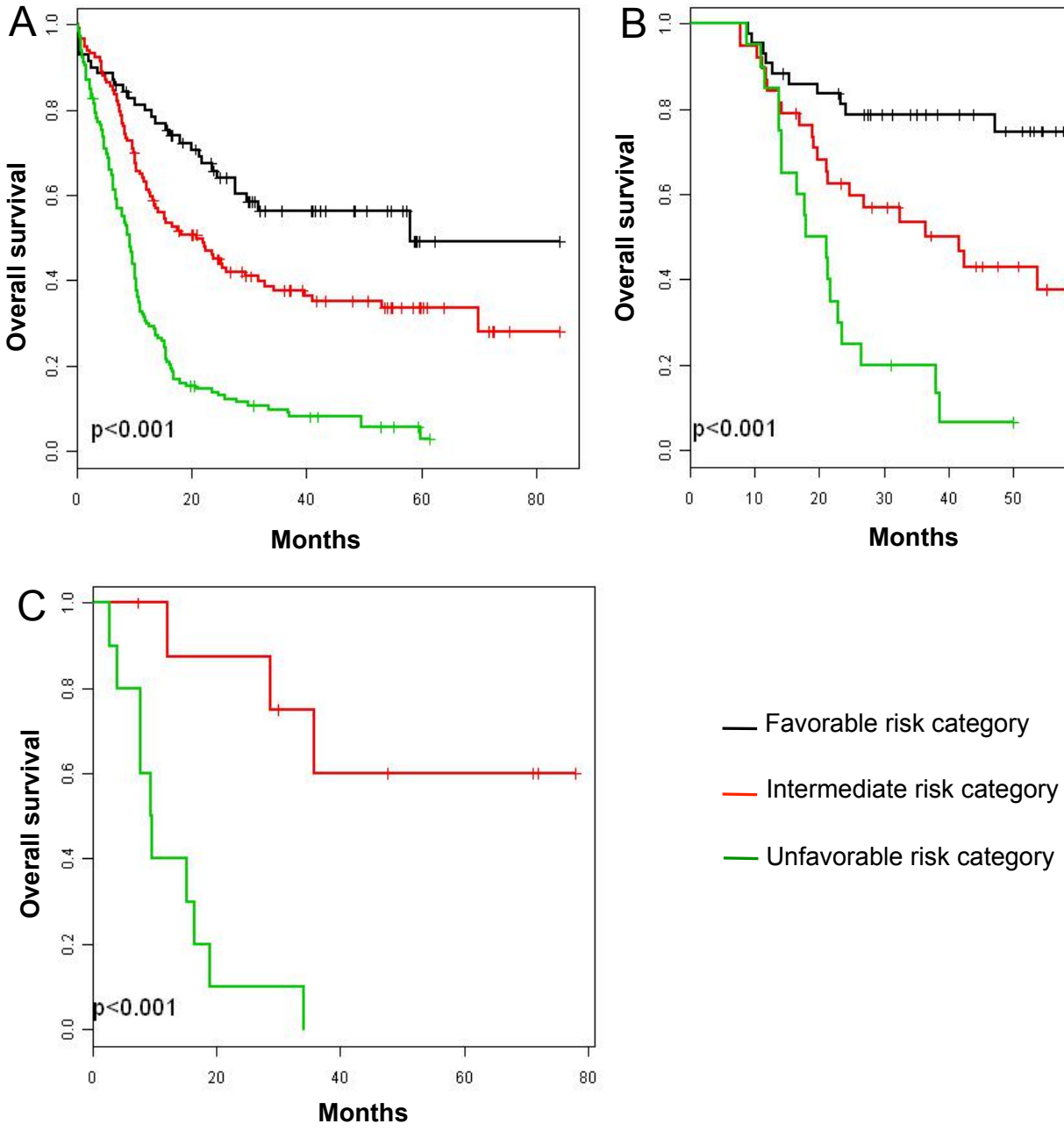

A
Overall survival
0.0
0.2
0.4
0.6
0.8
1.0
p<0.001
0
20
40
60
80
Months
B
Overall survival
0.0
0.2
0.4
0.6
0.8
1.0
p<0.001
0
10
20
30
40
50
60
70
Months
C
Overall survival
0.0
0.2
0.4
0.6
0.8
1.0
p<0.001
0
20
40
60
80
Months
Favorable risk category
Intermediate risk category
Unfavorable risk category

Figure S11

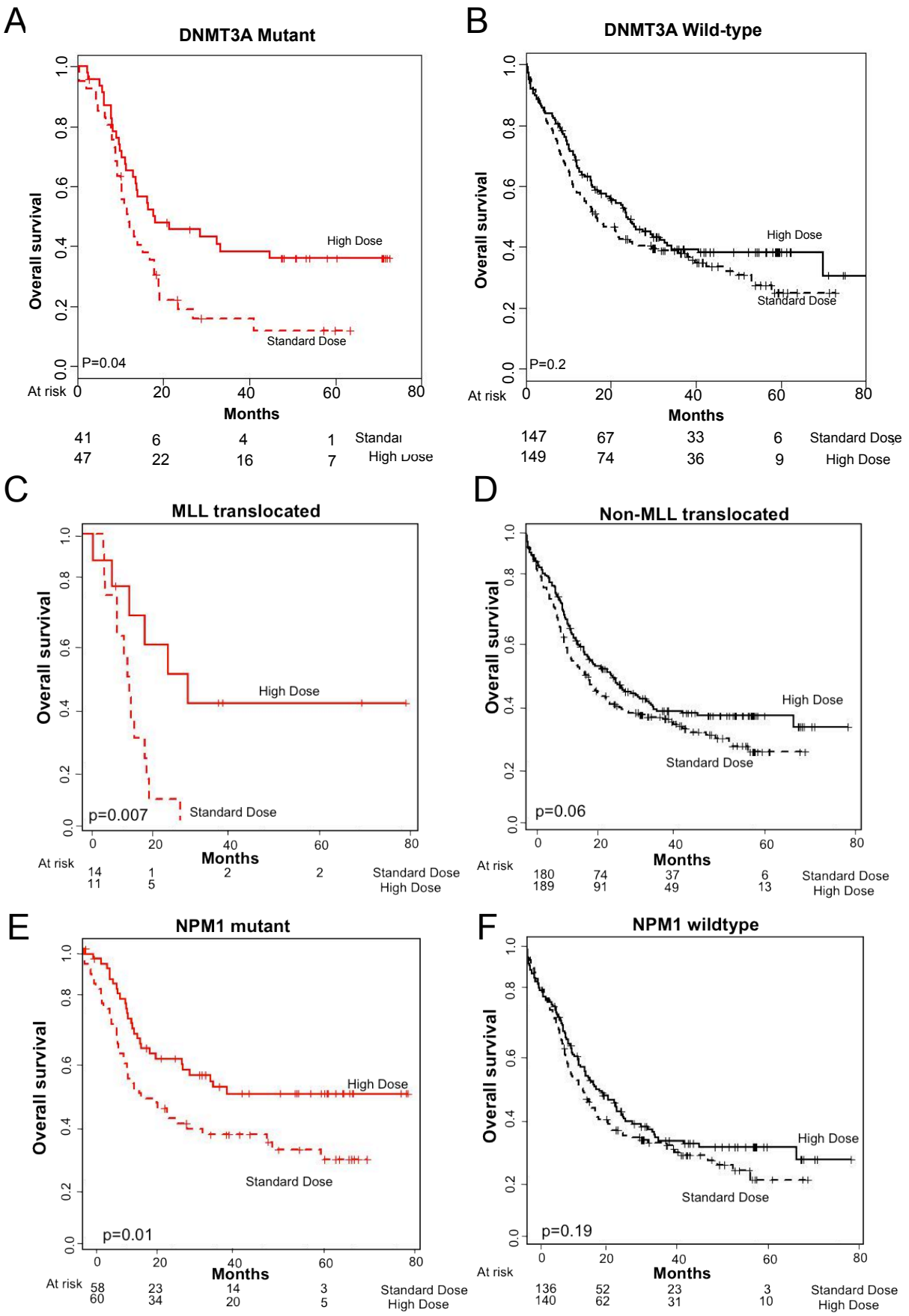

A
DNMT3A Mutant
Overall survival
High Dose
Standard Dose
P=0.04
At risk
Months
41 6 4 1 Standar
47 22 16 7 High Dose
B
DNMT3A Wild-type
Overall survival
High Dose
Standard Dose
P=0.2
At risk
Months
147 67 33 6 Standard Dose
149 74 36 9 High Dose
C
MLL translocated
Overall survival
High Dose
Standard Dose
p=0.007
At risk
Months
14 1 2 2 Standard Dose
11 5 High Dose
D
Non-MLL translocated
Overall survival
High Dose
Standard Dose
p=0.06
At risk
Months
180 74 37 6 Standard Dose
189 91 49 13 High Dose
E
NPM1 mutant
Overall survival
High Dose
Standard Dose
p=0.01
At risk
Months
58 23 14 3 Standard Dose
60 34 20 5 High Dose
F
NPM1 wildtype
Overall survival
High Dose
Standard Dose
p=0.19
At risk
Months
136 52 23 3 Standard Dose
140 62 31 10 High Dose

Table S1. Baseline characteristics of the 398 samples in the test cohort from the ECOG E1900 cohort and the entire cohort.

Variable	Test cohort (N = 398)	Validation cohort (N = 104)	Entire cohort (N=657)
Age			
Group – no (%)			
< 50yr	227 (57.0)	42 (40.8)	360 (54.8)
≥ 50 yr	171 (43.0)	61 (59.2)	297 (45.2)
Median- yr	46.5	53	48.0
Range- yr	18-60	18-60	17-60
Sex – no. (%)			
Male	207 (52.0)	51 (49.5)	335 (51.0)
Female	191 (48.0)	52 (50.5)	322 (49.0)
Peripheral blood white-cell count			
Level- no. (%)			
< 10,000/mm^3	123 (30.9)	84 (81.6)	306 (46.6)
≥ 10,000/mm^3	275 (69.1)	18 (17.5)	350 (53.3)
Missing data	0 (0)	1 (1)	1 (0.2)
Median- cells/mm^3 x 1000	19.9	2.5	12.3
Range - cells/mm^3 x 1000	1 – 213	1- 117	1 – 366
Hemoglobin			
Level – no. (%)			
<10g/dl	276 (69.3)	77 (74.8)	464 (70.6)
≥10g/dl	121 (30.4)	25 (24.3)	191 (29.1)
Missing data	1 (0.3)	1 (1)	2 (0.3)
Median – g/dl	9.2	9.2	9.2
Range – g/dl	5 - 30	5-14	5 – 30
Peripheral-blood platelet count			
Level – no. (%)			
<50,000/mm3	194 (48.7)	43 (41.7)	305 (46.4)
≥50,000/mm3	204 (51.3)	59 (57.3)	351 (53.4)
Missing data	0 (0)	1 (1)	1 (0.2)
Median – g/dl	50.0	61	50.0
Range – g/dl	1 - 650	6-995	1 – 995
Blasts			
Peripheral blood			
Median %	47.5	8	31
Range %	0-98	0-99	0-99
Bone Marrow			
Median %	68.5	49	64.0
Range %	3 - 100	17-100	3 - 100
Leukemia Classification – no (%)			
Not reviewed	0 (0)	0	21 (3.2)
AML Minimally Differentiated	20 (5.0)	5 (4.9)	29 (4.4)

AML w/o Maturation	96 (24.1)	22 (21.4)	155 (23.6)
AML w/ Maturation	61 (15.3)	27 (26.2)	112 (17.0)
Acute myelomonocytic Leukemia	52 (13.1)	7 (6.8)	63 (9.6)
Acute monocytic/monoblastic Leukemia	27 (6.8)	3 (2.9)	40 (6.1)
Acute erythroid Leukemia	8 (2.0)	6 (5.8)	29 (4.4)
Acute megakaryoblastic Leukemia	0 (0)	2 (1.9)	3 (0.5)
Cytogenetic profile – no. (%)			
Favorable	67 (16.8)	10 (9.7)	89 (13.5)
Indeterminate	85 (21.4)	22 (21.4)	176 (26.8)
Intermediate	180 (45.2)	42 (40.8)	267 (40.6)
Normal karyotype	163 (41.0)	42 (40.4)	244 (37.1)
Unfavorable	65 (16.3)	29 (28.2)	122 (18.6)
Patients with secondary AML	11/398 (2.8)	4 (3.9)	22/657 (3.3)
Survival (days)			
Median	535.2	650.9	621

Table S2: Genomic DNA primer sequences utilized for comprehensive genetic analysis. All primer sequences are displayed with M13F2/M13R2 tags.

Gene	Genomic coordinates of target region	Forward Primer Sequence	Reverse Primer Sequence
ASXL1	chr20:30410194-30410296	GTAAAACGACGGCCAGTGGTCCTGTCTCAGTCCCTCA	CAGGAAACAGCTATGACCTCTTAAAGGAAGATGGCCCC
	chr20:30417847-30417930	GTAAAACGACGGCCAGTCCAGCGGTACCTCATAGCAT	CAGGAAACAGCTATGACCGCGTTAGGCACAATAGAGGC
	chr20:30420478-30420587	GTAAAACGACGGCCAGTTGGATTTCGGGTATCACATAA	CAGGAAACAGCTATGACCtccaagaatcaCTGCACCAA
	chr20:30479591-30479712	GTAAAACGACGGCCAGTTCCCTCTTTTTCAAAAGCATACA	CAGGAAACAGCTATGACCACCCATCCATTAAAGGGTCC
	chr20:30479788-30479886	GTAAAACGACGGCCAGTTTGCTGTCACAGAAGGATGC	CAGGAAACAGCTATGACCTGTCATCATTCATCCTCCCA
	chr20:30480801-30480895	GTAAAACGACGGCCAGTAATGATGCTTGGCACAGTGA	CAGGAAACAGCTATGACCCAGAGCCCAGCACTAGAACC
	chr20:30481364-30481517	GTAAAACGACGGCCAGTGGTTCTAGTGCTGGGCTCTG	CAGGAAACAGCTATGACCAAAATAGAGGGCCACCCAAG
	chr20:30482784-30482948	GTAAAACGACGGCCAGTGCTTTGTGGAGCCTGTTCTC	CAGGAAACAGCTATGACCAGAAGGATCAAGGGGGAAAA
	chr20:30483046-30483143	GTAAAACGACGGCCAGTGTCAAATGAAGCGCAACAGA	CAGGAAACAGCTATGACCGGAGACATGCAACACCACAC
	chr20:30484343-30484449	GTAAAACGACGGCCAGTCAAGGAGTTGCTTGGTCTCA	CAGGAAACAGCTATGACCCACGTTCTGCTGCAATGACT
	chr20:30484747-30485127	GTAAAACGACGGCCAGTCGACAGGAAATGGAGAAGGA	CAGGAAACAGCTATGACCTTCTGATCCTTGGGTTCCTG
	chr20:30485128-30485381	GTAAAACGACGGCCAGTAAAAGTGGCTTGTGTGTCCC	CAGGAAACAGCTATGACCGGCTGTCTCAAGCAAACCTC
	chr20:30485895-30486275	GTAAAACGACGGCCAGTGAGGTTTGCTTGAGACAGCC	CAGGAAACAGCTATGACCGAAGGCAGGTCCTCTCTCCT
	chr20:30486276-30486655	GTAAAACGACGGCCAGTGGACCCTCGCAGACATTAAA	CAGGAAACAGCTATGACCTGTTCTGCAGGCAATCAGTC
	chr20:30486656-30487035	GTAAAACGACGGCCAGTGCCATGTCCAGAGCTAGGAG	CAGGAAACAGCTATGACCTGGCACAGTCCAGAGTGAAG
	chr20:30487036-30487415	GTAAAACGACGGCCAGTCTTGAAAACCAAGGCTCTCG	CAGGAAACAGCTATGACCCACAAGTGGGTTAGTGGCCT
	chr20:30487416-30487795	GTAAAACGACGGCCAGTCAAGGTGAATGGTGACATGC	CAGGAAACAGCTATGACCCTGGATGGAGGGAGTCAAAA
	chr20:30487796-30488175	GTAAAACGACGGCCAGTCTGAGTACCAGCCAAGAGCC	CAGGAAACAGCTATGACCAAGTGACCCACCAGTTCCAG
	chr20:30488176-30488555	GTAAAACGACGGCCAGTTTTTGACTCCCTCCATCCAG	CAGGAAACAGCTATGACCACACTGGAGCGAGATGCTTT
	chr20:30488556-30488935	GTAAAACGACGGCCAGTCTGGAACTGGTGGGTCACTT	CAGGAAACAGCTATGACCTATACCCAGGAAACCCCTCC
CEBPa	chr19:38483156-38483535	GTAAAACGACGGCCAGTGCAAGTATCCGAGCAAAACC	CAGGAAACAGCTATGACCGAGGAGGGGAGAATTCTTGG
	chr19:38483156-38483535	GTAAAACGACGGCCAGTCCGACGGAGAGTCTCATTTT	CAGGAAACAGCTATGACCCCTGCTATAGGCTGGGCTTC
	chr19:38483156-38483535	GTAAAACGACGGCCAGTGGAGAGGCGTGGAACTAGAG	CAGGAAACAGCTATGACCCTTGGTGCGTCTAAGATGAGG
	chr19:38483536-38483915	GTAAAACGACGGCCAGTTCATAACTCCGGTCCCTCTG	CAGGAAACAGCTATGACCCTGGAGCTGACCAGTGACAA
	chr19:38483916-38484295	GTAAAACGACGGCCAGTCATTTCCAAGGCACAAGGTT	CAGGAAACAGCTATGACCTGGACAAGAACAGCAACGAG
	chr19:38484296-38484675	GTAAAACGACGGCCAGTTTGTCACTGGTCAGCTCCAG	CAGGAAACAGCTATGACCCCTTCAACGACGAGTTCCTG
	chr19:38484296-38484675	GTAAAACGACGGCCAGTTTGTCACTGGTCAGCTCCAG	CAGGAAACAGCTATGACCCACCTGCAGTTCCAGATCG
	chr19:38484296-38484675	GTAAAACGACGGCCAGTCAGGTGCATGGTGGTCTG	CAGGAAACAGCTATGACCATCGACATCAGCGCCTACAT

	chr19:38484296-38484675	GTAAAACGACGGCCAGTCAGGTGCATGGTGGTCTG	CAGGAAACAGCTATGACCATCGACATCAGCGCCTACAT
	chr19:38484676-38485055	GTAAAACGACGGCCAGTCTCGTTGCTGTTCTTGTCCA	CAGGAAACAGCTATGACCCGGGAGAACTCTAACTCCCC
	chr19:38484676-38485055	GTAAAACGACGGCCAGTCTCGTTGCTGTTCTTGTCCA	CAGGAAACAGCTATGACCCAGGCTGGAGCCCCTGTA
	chr19:38484676-38485055	GTAAAACGACGGCCAGTGCTTGGCTTCATCCTCCTC	CAGGAAACAGCTATGACCTCGGCCGACTTCTACGAG
	chr19:38485056-38485160	GTAAAACGACGGCCAGTATGTAGGCGCTGATGTCGAT	CAGGAAACAGCTATGACCCGGGAGAACTCTAACTCCCC
DNMT3a	chr2:25310489-25310793	GTAAAACGACGGCCAGTCCTCTCTCCCACCTTTCCTC	CAGGAAACAGCTATGACCCTGAGTGCCGGGTTGTTTAT
	chr2:25312079-25312198	GTAAAACGACGGCCAGTGGAAAACAAGTCAGGTGGGA	CAGGAAACAGCTATGACCTGGATCTAAGATTGGCCAGG
	chr2:25313308-25313378	GTAAAACGACGGCCAGTccacactagctggagaagca	CAGGAAACAGCTATGACCggggctcttaccctgtgaac
	chr2:25315502-25315588	GTAAAACGACGGCCAGTcatggcagagcagctagtca	CAGGAAACAGCTATGACCtgtgtggctcctgagagaga
	chr2:25316674-25316823	GTAAAACGACGGCCAGTAATACCCAACCCCAGGAGTC	CAGGAAACAGCTATGACCCTTCCTGTCTGCCTCTGTCC
	chr2:25317012-25317103	GTAAAACGACGGCCAGTGAAGCCATTAGTGAGCTGGC	CAGGAAACAGCTATGACCCAACTTGGTCCCGTTCTTGT
	chr2:25317934-25318080	GTAAAACGACGGCCAGTTTGCCAAAAGTATTGGGAGG	CAGGAAACAGCTATGACCCCAGTTGGATCCAGAAAGGA
	chr2:25320270-25320355	GTAAAACGACGGCCAGTaagcttccccttgggataa	CAGGAAACAGCTATGACCcagggtgtgtgggtctagga
	chr2:25320527-25320711	GTAAAACGACGGCCAGTAGGGTCCTAAGCAGTGAGCA	CAGGAAACAGCTATGACCCGGTCTTTCCATTCCAGGTA
	chr2:25320912-25321025	GTAAAACGACGGCCAGTaggtgtgctacctggaatgg	CAGGAAACAGCTATGACCcagggcttaggctctgtgag
	chr2:25321625-25321705	GTAAAACGACGGCCAGTATCTGGGGACTAAAATGGGG	CAGGAAACAGCTATGACCCCTGGACTCTTTTCTGGCTG
	chr2:25322392-25322437	GTAAAACGACGGCCAGTAGCAAAGGTGAAAGGCTGAA	CAGGAAACAGCTATGACCAGCCCAAGGTCAAGGAGATT
	chr2:25322532-25322682	GTAAAACGACGGCCAGTTCCCAGGCAACAAACTTACC	CAGGAAACAGCTATGACCGAACAAGTTGGAGACCAGGC
	chr2:25322992-25323149	GTAAAACGACGGCCAGTTCTTCTGGAGGAGGAAAGCA	CAGGAAACAGCTATGACCCCTGTGCCACCCTCACTACT
	chr2:25323423-25323531	GTAAAACGACGGCCAGTAGTAGTGAGGGTGGCACAGG	CAGGAAACAGCTATGACCCTCCTCTTTGCATCGGGTAA
	chr2:25323963-25324122	GTAAAACGACGGCCAGTCTTACACTTGCAAGCACCCA	CAGGAAACAGCTATGACCGCCTCGTGACCACTGTGTAA
	chr2:25324409-25324625	GTAAAACGACGGCCAGTCATCCACCAAGACACAATGC	CAGGAAACAGCTATGACCCTGTCACTGTTCCGGGTTTT
	chr2:25326029-25326097	GTAAAACGACGGCCAGTTCTTCTCCACAATTCCCCTG	CAGGAAACAGCTATGACCAGGGCCGTGTTTCCTAGATT
	chr2:25328566-25328684	GTAAAACGACGGCCAGTCACTCTTTTCAAACCCGGAG	CAGGAAACAGCTATGACCgcgcTAATCTCTTCCAGAGC
	chr2:25351313-25351460	GTAAAACGACGGCCAGTactgaggcccatcacttctg	CAGGAAACAGCTATGACCcattgtgtttgaggcgagtg
	chr2:25351872-25351916	GTAAAACGACGGCCAGTCTTCCCACAGAGGGATGTGT	CAGGAAACAGCTATGACCgaaCAGCTAAACGGCCAGAG
	chr2:25358585-25358964	GTAAAACGACGGCCAGTTACAATCACCCAGCCCTCTC	CAGGAAACAGCTATGACCAGCGGTCAATGATCCAAAAC
	chr2:25358965-25359084	GTAAAACGACGGCCAGTAGCCAAGTCCCTGACTCTCA	CAGGAAACAGCTATGACCAGCGGTCAATGATCCAAAAC
	chr2:25376511-25376616	GTAAAACGACGGCCAGTTTGAAGAATGGGGTACCTGC	CAGGAAACAGCTATGACCGGTGGGGGCATATTACACAG
	chr2:25390285-25390534	GTAAAACGACGGCCAGTtgcggtcatgcaCTCAGTAT	CAGGAAACAGCTATGACCGATCCTCTTCTCTCCCCCAC
EZH2	chr7:148135407-	GTAAAACGACGGCCAGTcttccacatattcacaggcagt	CAGGAAACAGCTATGACCcttcagcaggctttgttgtg

	chr7:148137095-148137180	GTAAAACGACGGCCAGTGCGGCATGATATGAGAAGGT	CAGGAAACAGCTATGACCCGCAAGGGTAACAAAATTCG
	chr7:148137334-148137415	GTAAAACGACGGCCAGTtggtgtcagtgagcatgaaga	CAGGAAACAGCTATGACCttttagattttgtggtggatgc
	chr7:148138357-148138439	GTAAAACGACGGCCAGTCACAAGAGGTGAGGTGAGCA	CAGGAAACAGCTATGACCGTGACCCTTTTTGTTGCGTT
	chr7:148139649-148139745	GTAAAACGACGGCCAGTAGCATGCAAATCCACAAACA	CAGGAAACAGCTATGACCGTGTGCCCAATTACTGCCTT
	chr7:148141983-148142162	GTAAAACGACGGCCAGTTTTGCCCCAGCTAAATCATC	CAGGAAACAGCTATGACCgtacagcccttgccacgtaT
	chr7:148142938-148143064	GTAAAACGACGGCCAGTCCTGCCTCACACACACAGAC	CAGGAAACAGCTATGACCCTTGGGGGTGGGAGAGTATT
	chr7:148143530-148143571	GTAAAACGACGGCCAGTCGGCTACATCTCAGTCCCAT	CAGGAAACAGCTATGACCATTTGTAGCTTCCCGCAGAA
	chr7:148144708-148144803	GTAAAACGACGGCCAGTCCAACAACAGCCCTTAGGAA	CAGGAAACAGCTATGACCCCCAGCATCTAGCAGTGTCA
	chr7:148145246-148145416	GTAAAACGACGGCCAGTTGACACTGCTAGATGCTGGG	CAGGAAACAGCTATGACCGCCGATTGGATTTGAGTTGT
	chr7:148145901-148146142	GTAAAACGACGGCCAGTACAACTCAAATCCAATCGGC	CAGGAAACAGCTATGACCTGCCCTGATGTTGACATTTT
	chr7:148147620-148147712	GTAAAACGACGGCCAGTGAGAGGGGCTTGGGATCTAC	CAGGAAACAGCTATGACCTGCGCATCAGTTTTACTTGC
	chr7:148154478-148154657	GTAAAACGACGGCCAGTTCAGAGCAATCCTCAAGCAA	CAGGAAACAGCTATGACCTTCTTGATAACACCATGCACAA
	chr7:148155188-148155291	GTAAAACGACGGCCAGTAAGTGTAGTGGCTCATCCGC	CAGGAAACAGCTATGACCttctgcttcccagtgctctT
	chr7:148156764-148156905	GTAAAACGACGGCCAGTccaccctacctggccATAAT	CAGGAAACAGCTATGACCTGCTTCCTTTGCCTAACACC
	chr7:148157752-148157873	GTAAAACGACGGCCAGTGAGCCCCTATATGCCACAGA	CAGGAAACAGCTATGACCTGCTTATTGGTGAGAGGGGT
	chr7:148160658-148160775	GTAAAACGACGGCCAGTctgtcttgattcaccttgacaat	CAGGAAACAGCTATGACCggctacagcttaaggttgtcct
	chr7:148174494-148174623	GTAAAACGACGGCCAGTGGTCAATGATTTCCTCCCAA	CAGGAAACAGCTATGACCATGGCAATCGTTTCCTGTTC
	chr7:148175206-148175330	CAGGAAACAGCTATGACCATGGCAATCGTTTCCTGTTC	CAGGAAACAGCTATGACCgcagcacaaatgagcacct
FLT3	chr13:27490603-27490726	GTAAAACGACGGCCAGTCCTGAAGCTGCAGAAAAACC	CAGGAAACAGCTATGACCTCCATCACCGGTACCTCCTA
	chr13:27490603-27490726	GTAAAACGACGGCCAGTGTTGACACCCCAATCCACTC	CAGGAAACAGCTATGACCGTGACCGGCTCCTCAGATAA
	chr13:27506218-27506351	GTAAAACGACGGCCAGTTTTCCAAAAGCACCTGATCC	CAGGAAACAGCTATGACCTCATTGTCGTTTTAACCCTGC
HRAS	chr11:523765-523944	GTAAAACGACGGCCAGTGATCTGCTCCCTGAGAGGTG	CAGGAAACAGCTATGACCAGAGGCTGGCTGTGTGAACT
	chr11:523765-523944	GTAAAACGACGGCCAGTCTCCCTGGTACCTCTCATGC	CAGGAAACAGCTATGACCGTGGGTTTGCCCTTCAGAT
IDH1	chr2:208821337-208821629	GTAAAACGACGGCCAGTTGTGTTGAGATGGACGCCTA	CAGGAAACAGCTATGACCGGTGTACTCAGAGCCTTCGC
IDH2	chr15:88432822-88432983	GTAAAACGACGGCCAGTCTGCCTCTTTGTGGCCTAAG	CAGGAAACAGCTATGACCATTCTGGTTGAAAGATGGCG
JAK2	chr9:5063697-5063785	GTAAAACGACGGCCAGTGGGTTTCCTCAGAACGTTGA	CAGGAAACAGCTATGACCCTGACACCTAGCTGTGATCCTG
KIT	chr4:55284506-55284621	GTAAAACGACGGCCAGTTTCTGCCCTTTGAACTTGCT	CAGGAAACAGCTATGACCAAAGCCACATGGCTAGAAAAA
	chr4:55288338-55288465	GTAAAACGACGGCCAGTCCACACCCTGTTCACTCCTT	CAGGAAACAGCTATGACCTGGCAAACCTATCAAAAGGG
	chr4:55293992-55294115	GTAAAACGACGGCCAGTTGTGAACATCATTCAAGGCG	CAGGAAACAGCTATGACCTGTTCAGCATACCATGCAAA
KRas	chr12:25271434-25271613	GTAAAACGACGGCCAGTTGCATGGCATTAGCAAAGAC	CAGGAAACAGCTATGACCGGTGCTTAGTGGCCATTTGT
	chr12:25289474-	GTAAAACGACGGCCAGTCCAAGGAAAGTAAAGTTCCCA	CAGGAAACAGCTATGACCCGTCTGCAGTCAACTGGAAT

	25289596		
NPM1	chr5:170770135-170770493	GTAAAACGACGGCCAGTCTCGGGAGATGAAGTTGGAA	CAGGAAACAGCTATGACCactccagcctaggggaAAAA
NRas	chr1:115057943-115058122	GTAAAACGACGGCCAGTGTGGTAACCTCATTTCCCCA	CAGGAAACAGCTATGACCGGGACAAACCAGATAGGCAG
	chr1:115060193-115060321	GTAAAACGACGGCCAGTCAGGTTTTAGAAACTTCAGCAGC	CAGGAAACAGCTATGACCATTAATCCGGTGTTTTTGCG
PHF6	chrX:133339267-133339451	GTAAAACGACGGCCAGTggggcttagagtggcttaattt	CAGGAAACAGCTATGACCgtctctgttgctgccggtat
	chrX:133339700-133339802	GTAAAACGACGGCCAGTTCTGAAAACCAGAAGGTGGC	CAGGAAACAGCTATGACCGGATTTTGCTGGCTCAGAGA
	chrX:133355196-133355330	GTAAAACGACGGCCAGTACCAATTTGTTTTCCTTGACAGA	CAGGAAACAGCTATGACCCGAGCAGTACACTTCACCCA
	chrX:133355604-133355648	GTAAAACGACGGCCAGTACCACTGTGCATTGCATGAT	CAGGAAACAGCTATGACCTGAAAAGTGGCTGAAACGTG
	chrX:133375183-133375353	GTAAAACGACGGCCAGTCTGAAACATTGGGTGGCTTT	CAGGAAACAGCTATGACCTTGGGCTTTAGATCACAGGG
	chrX:133375518-133375662	GTAAAACGACGGCCAGTATGAACATGAACTGGAGCCC	CAGGAAACAGCTATGACCTTGGGCTTTAGATCACAGGG
	chrX:133376711-133376987	GTAAAACGACGGCCAGTTTAATCTTGGCTCCACACTGG	CAGGAAACAGCTATGACCGCTTGCAAATGCCTTGAAAT
	chrX:133378864-133379244	GTAAAACGACGGCCAGTtttcttgaaatacggcttacga	CAGGAAACAGCTATGACCccggcccagtgtatgtagtt
	chrX:133386896-133387276	GTAAAACGACGGCCAGTCCCATGTTTTAAATGGGCAC	CAGGAAACAGCTATGACCATGATGCTTGAGGGGAACAC
PTEN	chr10:89614098-89614406	GTAAAACGACGGCCAGTatcagctaccgccaagtcc	CAGGAAACAGCTATGACCgcaacctgaccagggttaaa
	chr10:89643761-89643846	GTAAAACGACGGCCAGTCTCCAGCTATAGTGGGGAAA	CAGGAAACAGCTATGACCCTGTATCCCCCTGAAGTCCA
	chr10:89675249-89675294	GTAAAACGACGGCCAGTCCATAGAAGGGGTATTTGTTGG	CAGGAAACAGCTATGACCTGCCAACAATGTTTTACCTCA
	chr10:89680782-89680826	GTAAAACGACGGCCAGTAAAGATTCAGGCAATGTTTGTT	CAGGAAACAGCTATGACCTCTCACTCGATAATCTGGATGAC
	chr10:89682749-89682988	GTAAAACGACGGCCAGTGGAATCCAGTGTTTCTTTTAAATACC	CAGGAAACAGCTATGACCGAAACCCAAAATCTGTTTTCCA
	chr10:89701854-89701996	GTAAAACGACGGCCAGTGGCTACGACCCAGTTACCAT	CAGGAAACAGCTATGACCTAAAACCCATTGCTTTTGGC
	chr10:89707589-89707756	GTAAAACGACGGCCAGTTGCTTGAGATCAAGATTGCAG	CAGGAAACAGCTATGACCGCCATAAGGCCTTTTCCTTC
	chr10:89710630-89710855	GTAAAACGACGGCCAGTGCAACAGATAACTCAGATTGCC	CAGGAAACAGCTATGACCTTTTGACGCTGTGTACATTGG
	chr10:89715023-89715403	GTAAAACGACGGCCAGTTGTTCATCTGCAAAATGGAAT	CAGGAAACAGCTATGACCTAAAACGGGAAAGTGCCATC
RUNX1	chr21:35086148-35086527	GTAAAACGACGGCCAGTCTTCCTGTTTGCTTTCCAGC	CAGGAAACAGCTATGACCCACGCGCTACCACACCTAC
	chr21:35086528-35086777	GTAAAACGACGGCCAGTACCACGTCGCTCTGGTTC	CAGGAAACAGCTATGACCATCCTCGTCCTCTTGGGAGT
	chr21:35093467-35093629	GTAAAACGACGGCCAGTAAGAAAATCAGTGCATGGGC	CAGGAAACAGCTATGACCACCCTGGTACATAGGCCACA
	chr21:35115824-35115863	GTAAAACGACGGCCAGTTGTTACGACGGTTTGCAGAG	CAGGAAACAGCTATGACCGGAAGGGAAGGGAAATCTTG
	chr21:35128576-35128768	GTAAAACGACGGCCAGTAGTTGGTCTGGGAAGGTGTG	CAGGAAACAGCTATGACCGGAAAGACAAGAAAAGCCCC
	chr21:35153640-35153745	GTAAAACGACGGCCAGTGCAACTTTTTGGCTTTACGG	CAGGAAACAGCTATGACCGGTAACTTGTGCTGAAGGGC
	chr21:35174723-35174880	GTAAAACGACGGCCAGTCCGAGTTTCTAGGGATTCCA	CAGGAAACAGCTATGACCCATTGCTATTCCTCTGCAACC
	chr21:35181009-35181389	GTAAAACGACGGCCAGTAGAAAGCTGAGACGAGTGCC	CAGGAAACAGCTATGACCGCAGAACCAGAACGTTTTCC
	chr21:35187091-35187130	GTAAAACGACGGCCAGTGGAATCAGCAGAAACAGCCT	CAGGAAACAGCTATGACCAACCACGTGCATAAGGAACA

	chr21:35343008-35343388	GTAAAACGACGGCCAGTGGTGAAACAAGCTGCCATTT	CAGGAAACAGCTATGACCTTTGGGCCTCATAAACAACC
TET2	chr4:106374502-106374882	GTAAAACGACGGCCAGTCACCCTTGTTCTCCATGACC	CAGGAAACAGCTATGACCTGGTTGACTGCTTTCACCTG
	chr4:106374883-106375262	GTAAAACGACGGCCAGTAAATGGAGACACCAAGTGGC	CAGGAAACAGCTATGACCGAGGTATGCGATGGGTGAGT
	chr4:106375263-106375642	GTAAAACGACGGCCAGTATGAGCAGGAGGGGAAAAGT	CAGGAAACAGCTATGACCTGGTGTGGTAGTGGCAGAAA
	chr4:106375643-106376022	GTAAAACGACGGCCAGTACTCACCCATCGCATACCTC	CAGGAAACAGCTATGACCAGATAGTGCTGTGTTGGGGG
	chr4:106376023-106376402	GTAAAACGACGGCCAGTTTCCACAGGTTCCTCAGCTT	CAGGAAACAGCTATGACCGAGAAGTGCACCTGGTGTGA
	chr4:106376783-106377162	GTAAAACGACGGCCAGTAAGGCAAGCTTACACCCAGA	CAGGAAACAGCTATGACCGGTTCCACCTTAATTGGCCT
	chr4:106377163-106377542	GTAAAACGACGGCCAGTAATGTCCAAATGGGACTGGA	CAGGAAACAGCTATGACCACTGGCCCTGACATTTCAAC
	chr4:106377543-106377922	GTAAAACGACGGCCAGTCCCCAGAAGGACACTCAAAA	CAGGAAACAGCTATGACCCAAATTGCTGCCAGACTCAA
	chr4:106377923-106378302	GTAAAACGACGGCCAGTACTTGATAGCCACACCCCAG	CAGGAAACAGCTATGACCTTCCCCCAACTCATGAAGAC
	chr4:106381723-106382102	GTAAAACGACGGCCAGTtgcacaaaaggtagaatgcaa	CAGGAAACAGCTATGACCacgtgggatttcacacaaca
	chr4:106383439-106383533	GTAAAACGACGGCCAGTTTTCCCATTTTCACCCACAT	CAGGAAACAGCTATGACCACCCAATTCTCAGGGTCAGA
	chr4:106384175-106384384	GTAAAACGACGGCCAGTAGGGTCAAAGCCCACTTTTT	CAGGAAACAGCTATGACCTGAGGCCATGTGGTTACAGA
	chr4:106400224-106400375	GTAAAACGACGGCCAGTGTGTGGTTATGCCACAGCTT	CAGGAAACAGCTATGACCCCAAAGAGGAAGTTTTTGTTGC
	chr4:106402364-106402454	GTAAAACGACGGCCAGTACCATACGGCTTAATTCCCC	CAGGAAACAGCTATGACCTGTTACAATTGCTGCCAATGA
	chr4:106410215-106410353	GTAAAACGACGGCCAGTTGTCATTCCATTTTGTTTCTGG	CAGGAAACAGCTATGACCCTGCTAAGCTGTCCTCAGCC
	chr4:106413169-106413524	GTAAAACGACGGCCAGTTCTGGATCAACTAGGCCACC	CAGGAAACAGCTATGACCGGGGGCAAAACCAAAATAAT
	chr4:106415653-106416033	GTAAAACGACGGCCAGTTCAAGCAGAGGCATGTTCAG	CAGGAAACAGCTATGACCTATTTCCAAACCTTGGCTGG
	chr4:106416034-106416413	GTAAAACGACGGCCAGTAATCCCATGAACCCTTACCC	CAGGAAACAGCTATGACCACCAGACCTCATCGTTGTCC
	chr4:106416414-106416793	GTAAAACGACGGCCAGTATCAGTGGACAACTGCTCCC	CAGGAAACAGCTATGACCATGAAACGCAGGTAAGTGGG
	chr4:106416794-106417173	GTAAAACGACGGCCAGTATTGGCACTAGTCCAGGGTG	CAGGAAACAGCTATGACCACTGTGACCTTTCCCCACTG
TP53	chr17:7505821-7506057	GTAAAACGACGGCCAGTCGGAACTCCTGAGCTGAAAG	CAGGAAACAGCTATGACCGCAGGAGAGTTGCTTGAACC
	chr17:7510128-7510287	GTAAAACGACGGCCAGTGTGCTGTGTGCTGGGATTAC	CAGGAAACAGCTATGACCGTGCCAGGAGCTGTTCTAGG
	chr17:7513585-7513733	GTAAAACGACGGCCAGTCCACAACAAAACACCAGTGC	CAGGAAACAGCTATGACCAAAGCATTGGTCAGGGAAAA
	chr17:7514651-7514758	GTAAAACGACGGCCAGTTCAACCGGAGGAAGACTAAAAA	CAGGAAACAGCTATGACCATCAGCCAAGATTGCACCAT
	chr17:7517249-7517309	GTAAAACGACGGCCAGTaagcaggctaggctaagctatg	CAGGAAACAGCTATGACCaaggaccagaccagctttca
	chr17:7517577-7517651	GTAAAACGACGGCCAGTTGTCTTTGAGGCATCACTGC	CAGGAAACAGCTATGACCGCGCACAGAGGAAGAGAATC
	chr17:7517743-7517880	GTAAAACGACGGCCAGTGTGGTTTCTTCTTTGGCTGG	CAGGAAACAGCTATGACCCAAGGGTGGTTGGGAGTAGA
	chr17:7518223-7518333	GTAAAACGACGGCCAGTtggaagaaatcggtaagaggtg	CAGGAAACAGCTATGACCctgcttgccacaggtctcc

	chr17:7518223-7518333	GTAAAACGACGGCCAGTtggaagaaatcggtaagaggtg	CAGGAAACAGCTATGACCctgcttgccacaggtctcc
	chr17:7518901-7519014	GTAAAACGACGGCCAGTTTGCACATCTCATGGGGTTA	CAGGAAACAGCTATGACCAGTCACAGCACATGACGGAG
	chr17:7519095-7519475	GTAAAACGACGGCCAGTTTACCTGCAATTGGGGCATT	CAGGAAACAGCTATGACCGCAGGCTAGGCTAAGCTATGATG
	chr17:7520036-7520315	GTAAAACGACGGCCAGTGCCAAAGGGTGAAGAGGAAT	CAGGAAACAGCTATGACCGTAAGGACAAGGGTTGGGCT
	chr17:7520424-7520446	GTAAAACGACGGCCAGTTCATCTGGACCTGGGTCTTC	CAGGAAACAGCTATGACCCCCCTCTGAGTCAGGAAACA
	chr17:7520563-7520665	GTAAAACGACGGCCAGTAGCCCAACCCTTGTCCTTAC	CAGGAAACAGCTATGACCCAGCCATTCTTTTCCTGCTC
WT1	chr11:32367041-32367301	GTAAAACGACGGCCAGTGGGGACATGATCAGCTATGG	CAGGAAACAGCTATGACCTCCTTAAAGCCCCAAGAGGT
	chr11:32370093-32370186	CAGGAAACAGCTATGACCGCCACGCACTATTCCTTCTC	GTAAAACGACGGCCAGTGGGAAATCTAAGGGTGAGGC
	chr11:32370787-32370877	CAGGAAACAGCTATGACCTGTGGGGTGTTTCCTTTTCT	GTAAAACGACGGCCAGTGTTGGGGATCATCCTACCCT
	chr11:32374378-32374529	CAGGAAACAGCTATGACCTAGCAGTGTGAGAGCCTGGA	GTAAAACGACGGCCAGTGGAGTGTGAATGGGAGTGGT
	chr11:32378069-32378166	CAGGAAACAGCTATGACCTAAGGAACTAAAGGGCCGGT	GTAAAACGACGGCCAGTCCATCATTCCCTCCTGATTG
	chr11:32394611-32394662	CAGGAAACAGCTATGACCGAATAAGAAGAGGTGGGGGC	GTAAAACGACGGCCAGTGGCTTTTCACTGGATTCTGG
	chr11:32395698-32395776	CAGGAAACAGCTATGACCACCAACTAGGGGAAGGAGGA	GTAAAACGACGGCCAGTCTGTGCAGAGATCAGTGGGA
	chr11:32406077-32406180	GTAAAACGACGGCCAGTCAGAGACCAGGGAGATCAGC	GTAAAACGACGGCCAGTGACTGCTAGGGGAATGCAAA
	chr11:32406618-32406741	GTAAAACGACGGCCAGTTGCCATTGGGGTAATGATTT	CAGGAAACAGCTATGACCCAAGGTCACATCCAGGGACT
	chr11:32408651-32408935	GTAAAACGACGGCCAGTAGTGAAGGCCGAATTTCTGA	CAGGAAACAGCTATGACCTCCAAGGCCTGTACAAGGAG
	chr11:32412821-32413201	GTAAAACGACGGCCAGTGGTAAGAGCTGCGGTCAAAA	CAGGAAACAGCTATGACCCTACAGCAGCCAGAGCAGC
	chr11:32413202-	GTAAAACGACGGCCAGTGGCTCCTGTTTGATGAAGGA	CAGGAAACAGCTATGACCGTAAGGAGTTCAAGGCAGCG

Table S3. P-values for the test of proportional hazards for all mutations identified in the Test cohort.

Gene	p-value
DNMT3A	0.17
IDH1	0.24
IDH2	0.59
IDH2R140Q	0.61
IDH2R172K	0.13
TET2	0.92
ASXL1	0.16
FLT3	0.6
NPM1	0.23
PHF6	0.09
KIT	0.24
CEBPA	0.23
WT1	0.68
KRas	0.45
NRas	0.49
P53	0.85
PTEN	0.95
RUNX1	0.09
CBF	0.67
Del(5q)	0.66
EVI	0.9
MLL-PTD	0.04
Split MLL	0.21
Monosomy 7	0.97
t(6;9)	0.36
Trisomy 8	0.89
AML1-ETO	0.08

Table S4. Mutational frequency of genes sequenced in patients in the overall ECOG E1900 cohort and within each cytogenetic risk group.

Gene	Overall Frequency (%)	Favorable Risk	Intermediate Risk	Unfavorable Risk
FLT3 (ITD, TKD)[1]	37 (30, 7)	8 (3, 5)	52 (42, 7)*	36 (35, 1)
NPM1	29	4	49*	12
DNMT3A	23	4	33*	15
NRAS	10	12	5	2
CEBPA	9	5	12	5
TET2	8	5	8	10
WT1	8	1	12*	5
IDH2	8	3	9	9
IDH1	7	3	9	3
KIT	6	28*	1	0
RUNX1	5	3	6	6
MLL-PTD[2]	5	0	5	8
ASXL1	3	0	4	2
PHF6	3	1	2	3
KRAS	2	7	5	3
PTEN	2	1	2	1
TP53	2	0	1	6
HRAS	0	0	0	0
EZH2	0	0	0	0

1) ITD – internal tandem duplication; TKD – tyrosine kinase domain mutation.
2) PTD – partial tandem duplication.
* denotes mutations which were significantly enriched in a specific cytogenetic risk group compared to the entire cohort ($p<0.01$ for all).

Table S5: Co-occurrences of somatic mutations and cytogenetic abnormalities in the test cohort of 398 AML patients with *de novo* AML from the ECOG E1900 trial.

	DNMT3a	IDH1	IDH2	TET2	ASXL1	FLT3	NPM1	CEBPA	WT1	KRas	NRas	PHF6	KIT	TP53	PTEN	RUNX1	CBF	Del (5q)	EVI1	MLL-PTD	Split MLL	Monosomy (7/7q)	t(6;9)	Tri(8)	AML1-ETO
DNMT3a		3.3% (13/398)	1.5% (6/398)	1.5% (6/398)	0% (0/398)	13.3% (53/398)	14.3% (57/398)	1.75% (7/398)	0.75% (3/398)	0.75% (3/398)	2.5% (10/398)	0% (0/398)	0.5% (2/398)	0.25% (1/398)	0.75% (3/398)	0.75% (3/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	1% (4/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	1.5% (6/398)	0% (0/398)
IDH1	3.3% (13/398)		0% (0/398)	0% (0/398)	0.25% (1/398)	1% (4/398)	1.5% (6/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0.75% (3/398)	0.5% (2/398)	0.25% (1/398)	0% (0/398)	0.5% (2/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0.5% (2/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0.5% (2/398)	0% (0/398)
IDH2	1.5% (6/398)	0% (0/398)		0% (0/398)	0.5% (2/398)	2% (8/398)	2% (8/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.75% (3/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.75% (3/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.75% (3/398)	0.5% (2/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)
TET2	1.5% (6/398)	0% (0/398)	0% (0/398)		0.75% (3/398)	3% (12/398)	1.5% (6/398)	0.5% (2/398)	0.5% (2/398)	0% (0/398)	1% (4/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	1.3% (5/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)
ASXL1	0% (0/398)	0.25% (1/398)	0.5% (2/398)	0.75% (3/398)		0% (0/398)	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	1% (4/398)	1.3% (5/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)
FLT3	13.3% (53/398)	1% (4/398)	2% (8/398)	3% (12/398)	0% (0/398)		6.8% (27/398)	3.5% (14/398)	5% (20/398)	0.25% (1/398)	0.5% (2/398)	1% (4/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)	1.5% (6/398)	1.5% (6/398)	0.25% (1/398)	0.25% (1/398)	2.5% (10/398)	0.5% (2/398)	0% (0/398)	0.25% (1/398)	2.26% (9/398)	0% (0/398)
NPM1	14.3% (57/398)	1.5% (6/398)	2% (8/398	1.5% (6/398)	0.25% (1/398)	6.8% (27/398)		0.5% (2/398)	0.25% (1/398)	0.5% (2/398)	1.3% (5/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.5% (2/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)
CEBPA	1.75% (7/398)	0.25% (1/398)	0% (0/398)	0.5% (2/398)	0.5% (2/398)	3.5% (14/398)	0.5% (2/398)		1.3% (5/398)	0% (0/398)	0.5% (2/398)	0.5% (2/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0% (0/398)	1% (4/398)	0% (0/398)	0% (0/398)	0.5% (2/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)
WT1	0.75% (3/398)	0% (0/398)	0% (0/398)	0.5% (2/398)	0% (0/398)	5% (20/398)	0.25% (1/398)	1.3% (5/398)		0% (0/398)	0.75% (3/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.75% (3/398)	1% (4/398)	0% (0/398)	0% (0/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)
KRas	0.75% (3/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0% (0/398)		0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0% (0/398	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
NRas	2.5% (10/398)	0.75% (3/398)	0.75% (3/398)	1% (4/398)	0.25% (1/398)	0.5% (2/398)	1.3% (5/398)	0.5% (2/398)	0.75% (3/398)	0% (0/398)		0% (0/398)	0.25% (1/398)	0% (0/398)	0.5% (2/398)	0.5% (2/398)	3% (12/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.75% (3/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
PHF6	0% (0/398)	0.5% (2/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	1% (4/398)	0% (0/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0% (0/398)		0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
KIT	0.5% (2/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)		0% (0/398)	0% (0/398)	0% (0/398)	5.3% (21/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
TP53	0.25% (1/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)		0.25% (1/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
PTEN	0.75% (3/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.5% (2/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0.25% (1/398)		0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
RUNX1	0.75% (3/398)	0.25% (1/398)	0.75% (3/398)	0.25% (1/398)	1% (4/398)	1.5% (6/398)	0.5% (2/398)	0% (0/398)	0.75% (3/398	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)		0.5% (2/398)	0.75% (3/398)	0% (0/398)	1% (4/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)
CBF	0.25% (1/398)	0.25% (1/398)	0% (0/398)	1.3% (5/398)	1.3% (5/398)	1.5% (6/398)	0% (0/398)	1% (4/398)	1% (4/398)	0.5% (2/398)	3% (12/398)	0.25% (1/398)	5.3% (21/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)		0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)
Del (5q)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.75% (3/398)	0% (0/398)		0% (0/398)	1% (4/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
EVI1	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)		0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
MLL-PTD	1% (4/398)	0.5% (2/398)	0.75% (3/398)	0% (0/398)	0.5% (2/398)	2.5% (10/398)	0% (0/398)	0.5% (2/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	1% (4/398)	0% (0/398)	1% (4/398)	0% (0/398)		0.5% (2/398)	0.25% (1/398)	0% (0/398)	0.25% (1/398)	0% (0/398)
Split MLL	0.25% (1/398)	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0.25% (1/398)	0.5% (2/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.75% (3/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)		0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)
Monosomy (7/7q)	0.25% (1/398)	0.25% (1/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)		0% (0/398)	0% (0/398)	0% (0/398)
t(6;9)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)		0% (0/398)	0% (0/398)
Tri(8)	1.5% (6/398)	0.5% (2/398)	0% (0/398)	0.25% (1/398)	0.25% (1/398)	2.26% (9/398)	0.25% (1/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)		0% (0/398)
AML1-ETO	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0.25% (1/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	0% (0/398)	

Table S6: Pairwise correlations between all genetic abnormalities.[1]

	Abnormality #1	Abnormality #2	M/M[2]	WT/M[3]	M/W[4]	WT/WT[5]
1	DNMT3A	IDH	19	32	70	262
2	DNMT3A	IDH1	13	9	76	286
3	DNMT3A	IDH2	6	23	83	272
4	DNMT3A	IDH2_R140Q	3	18	86	277
5	DNMT3A	IDH2_R172K	3	5	86	290
6	DNMT3A	TET2	6	26	83	266
7	DNMT3A	ASXL1	0	10	88	285
8	DNMT3A	FLT3	52	92	37	204
9	DNMT3A	NPM1	57	57	32	239
10	DNMT3A	PHF6	0	9	88	284
11	DNMT3A	KIT	2	21	87	275
12	DNMT3A	CEBPa	6	26	82	267
13	DNMT3A	WT1	3	26	86	264
14	DNMT3A	KRAS	2	6	87	288
15	DNMT3A	NRAS	10	28	79	267
16	DNMT3A	TP53	1	7	86	283
17	DNMT3A	PTEN	3	2	86	293
18	DNMT3A	RUNX1	3	16	85	267
19	DNMT3A	CBF	1	71	88	225
20	DNMT3A	del5q	1	5	88	291
21	DNMT3A	EVI1pos	0	5	89	291
22	DNMT3A	MLLPTD or split MLLPTD	4	13	85	283
23	DNMT3A	splitMLLPTD or split MLL	1	21	88	275
24	DNMT3A	MLLPTD or split MLL	5	32	84	264
25	DNMT3A	Monosomy7	1	2	88	294
26	DNMT3A	t(6;9)	0	2	89	294
27	DNMT3A	trisomy 8	6	9	83	287
28	DNMT3A	AML1ETO	0	1	89	295
29	DNMT3A_R882	IDH	13	38	50	282
30	DNMT3A_R882	IDH1	9	13	54	308
31	DNMT3A_R882	IDH2	4	25	59	296
32	DNMT3A_R882	IDH2_R140Q	2	19	61	302
33	DNMT3A_R882	IDH2_R172K	2	6	61	315
34	DNMT3A_R882	IDH1_IDH2_R172K	11	19	52	302
35	DNMT3A_R882	TET2	4	28	59	290
36	DNMT3A_R882	ASXL1	0	10	62	311
37	DNMT3A_R882	FLT3	41	103	22	219

38	DNMT3A_R882	NPM1	43	71	20	251
39	DNMT3A_R882	PHF6	0	9	62	310
40	DNMT3A_R882	KIT	2	21	61	301
41	DNMT3A_R882	CEBPa	4	28	58	291
42	DNMT3A_R882	WT1	0	29	63	287
43	DNMT3A_R882	KRAS	2	6	61	314
44	DNMT3A_R882	NRAS	5	33	58	288
45	DNMT3A_R882	TP53	1	7	60	309
46	DNMT3A_R882	PTEN	2	3	61	318
47	DNMT3A_R882	RUNX1	2	17	61	291
48	DNMT3A_R882	CBF	0	72	63	250
49	DNMT3A_R882	del5q	1	5	62	317
50	DNMT3A_R882	EVI1pos	0	5	63	317
51	DNMT3A_R882	MLLPTD or split MLLPTD	3	14	60	308
52	DNMT3A_R882	splitMLLPTD or split MLL	0	22	63	300
53	DNMT3A_R882	MLLPTD or split MLL	3	34	60	288
54	DNMT3A_R882	Monosomy7	0	3	63	319
55	DNMT3A_R882	t(6;9)	0	2	63	320
56	DNMT3A_R882	trisomy 8	5	10	58	312
57	DNMT3A_R882	AML1ETO	0	1	63	321
58	DNMT3A_other	IDH	6	45	22	310
59	DNMT3A_other	IDH1	4	18	24	338
60	DNMT3A_other	IDH2	2	27	26	329
61	DNMT3A_other	IDH2_R140Q	1	20	27	336
62	DNMT3A_other	IDH2_R172K	1	7	27	349
63	DNMT3A_other	IDH1_IDH2_R172K	5	25	23	331
64	DNMT3A_other	TET2	2	30	26	323
65	DNMT3A_other	ASXL1	0	10	28	345
66	DNMT3A_other	FLT3	12	132	16	225
67	DNMT3A_other	NPM1	15	99	13	258
68	DNMT3A_other	PHF6	0	9	28	344
69	DNMT3A_other	KIT	0	23	28	334
70	DNMT3A_other	CEBPa	2	30	26	323
71	DNMT3A_other	WT1	3	26	25	325
72	DNMT3A_other	KRAS	0	8	28	347
73	DNMT3A_other	NRAS	6	32	22	324
74	DNMT3A_other	TP53	0	8	28	341
75	DNMT3A_other	PTEN	1	4	27	352
76	DNMT3A_other	RUNX1	2	17	25	327

77	DNMT3A_other	CBF	1	71	27	286
78	DNMT3A_other	del5q	1	5	27	352
79	DNMT3A_other	EVI1pos	0	5	28	352
80	DNMT3A_other	MLLPTD or split MLLPTD	1	16	27	341
81	DNMT3A_other	splitMLLPTD or split MLL	1	21	27	336
82	DNMT3A_other	MLLPTD or split MLL	2	35	26	322
83	DNMT3A_other	Monosomy7	1	2	27	355
84	DNMT3A_other	t(6;9)	0	2	28	355
85	DNMT3A_other	trisomy 8	1	14	27	343
86	DNMT3A_other	AML1ETO	0	1	28	356
87	IDH	TET2	0	33	56	301
88	IDH	ASXL1	3	7	54	329
89	IDH	FLT3	13	133	44	205
90	IDH	NPM1	31	87	26	251
91	IDH	PHF6	2	7	54	328
92	IDH	KIT	1	22	56	316
93	IDH	CEBPa	1	33	56	302
94	IDH	WT1	0	30	56	303
95	IDH	KRAS	1	7	56	329
96	IDH	NRAS	6	34	51	303
97	IDH	TP53	0	8	57	323
98	IDH	PTEN	2	4	55	333
99	IDH	RUNX1	4	16	52	308
100	IDH	CBF	1	71	56	267
101	IDH	del5q	0	6	57	332
102	IDH	EVI1pos	0	5	57	333
103	IDH	MLLPTD or split MLLPTD	5	13	52	325
104	IDH	splitMLLPTD or split MLL	2	19	55	319
105	IDH	MLLPTD or split MLL	6	31	51	307
106	IDH	Monosomy7	2	2	55	336
107	IDH	t(6;9)	0	2	57	336
108	IDH	trisomy 8	2	13	55	325
109	IDH	AML1ETO	0	1	57	337
110	IDH1	IDH2	0	33	24	338
111	IDH1	IDH2_R140Q	0	24	24	347
112	IDH1	IDH2_R172K	0	9	24	362
113	IDH1	TET2	0	33	24	334

114	IDH1	ASXL1	1	9	23	361
115	IDH1	FLT3	4	142	20	230
116	IDH1	NPM1	14	104	10	268
117	IDH1	PHF6	2	7	21	362
118	IDH1	KIT	1	22	23	350
119	IDH1	CEBPa	1	33	23	336
120	IDH1	WT1	0	30	23	337
121	IDH1	KRAS	1	7	23	363
122	IDH1	NRAS	3	37	21	334
123	IDH1	TP53	0	8	24	356
124	IDH1	PTEN	2	4	22	367
125	IDH1	RUNX1	1	19	22	339
126	IDH1	CBF	1	71	23	301
127	IDH1	del5q	0	6	24	366
128	IDH1	EVI1pos	0	5	24	367
129	IDH1	MLLPTD or split MLLPTD	2	16	22	356
130	IDH1	splitMLLPTD or split MLL	0	21	24	351
131	IDH1	MLLPTD or split MLL	2	35	22	337
132	IDH1	Monosomy7	1	3	23	369
133	IDH1	t(6;9)	0	2	24	370
134	IDH1	trisomy 8	2	13	22	359
135	IDH1	AML1ETO	0	1	24	371
136	IDH2	ASXL1	2	8	31	353
137	IDH2	FLT3	9	138	24	225
138	IDH2	NPM1	17	101	16	262
139	IDH2	PHF6	0	9	33	350
140	IDH2	KIT	0	23	33	340
141	IDH2	CEBPa	0	34	33	325
142	IDH2	WT1	0	30	33	327
143	IDH2	KRAS	0	8	33	353
144	IDH2	NRAS	3	37	30	325
145	IDH2	TP53	0	8	33	348
146	IDH2	PTEN	0	6	33	356
147	IDH2	RUNX1	3	17	30	331
148	IDH2	CBF	0	72	33	291
149	IDH2	del5q	0	6	33	357
150	IDH2	EVI1pos	0	5	33	358
151	IDH2	MLLPTD or split MLLPTD	3	15	30	348
152	IDH2	splitMLLPTD or	2	20	31	343

		split MLL				
153	IDH2	MLLPTD or split MLL	4	34	29	329
154	IDH2	Monosomy7	1	3	32	360
155	IDH2	t(6;9)	0	2	33	361
156	IDH2	Trisomy 8	0	15	33	348
157	IDH2	AML1ETO	0	1	33	362
158	IDH2_R140Q	IDH2_R172K	0	9	24	363
159	IDH2_R140Q	TET2	0	33	23	335
160	IDH2_R140Q	ASXL1	1	9	23	361
161	IDH2_R140Q	FLT3	8	139	16	233
162	IDH2_R140Q	NPM1	16	102	8	270
163	IDH2_R140Q	PHF6	0	9	24	359
164	IDH2_R140Q	KIT	0	23	24	349
165	IDH2_R140Q	CEBPa	0	34	24	334
166	IDH2_R140Q	WT1	0	30	24	336
167	IDH2_R140Q	KRAS	0	8	24	362
168	IDH2_R140Q	NRAS	3	37	21	334
169	IDH2_R140Q	TP53	0	8	24	357
170	IDH2_R140Q	PTEN	0	6	24	365
171	IDH2_R140Q	RUNX1	2	18	22	339
172	IDH2_R140Q	CBF	0	72	24	300
173	IDH2_R140Q	del5q	0	6	24	366
174	IDH2_R140Q	EVI1pos	0	5	24	367
175	IDH2_R140Q	MLLPTD or split MLLPTD	1	17	23	355
176	IDH2_R140Q	splitMLLPTD or split MLL	2	20	22	352
177	IDH2_R140Q	MLLPTD or split MLL	2	36	22	336
178	IDH2_R140Q	Monosomy7	1	3	23	369
179	IDH2_R140Q	t(6;9)	0	2	24	370
180	IDH2_R140Q	trisomy 8	0	15	24	357
181	IDH2_R140Q	AML1ETO	0	1	24	371
182	IDH2_R172K	TET2	0	33	9	349
183	IDH2_R172K	ASXL1	1	9	8	376
184	IDH2_R172K	FLT3	1	146	8	241
185	IDH2_R172K	NPM1	1	117	8	270
186	IDH2_R172K	PHF6	0	9	9	374
187	IDH2_R172K	KIT	0	23	9	364
188	IDH2_R172K	CEBPa	0	34	9	349
189	IDH2_R172K	WT1	0	30	9	351
190	IDH2_R172K	KRAS	0	8	9	377

191	IDH2_R172K	NRAS	0	40	9	346
192	IDH2_R172K	TP53	0	8	9	372
193	IDH2_R172K	PTEN	0	6	9	380
194	IDH2_R172K	RUNX1	1	19	8	353
195	IDH2_R172K	CBF	0	72	9	315
196	IDH2_R172K	del5q	0	6	9	381
197	IDH2_R172K	EVI1pos	0	5	9	382
198	IDH2_R172K	MLLPTD or split MLLPTD	2	16	7	371
199	IDH2_R172K	splitMLLPTD or split MLL	0	22	9	365
200	IDH2_R172K	MLLPTD or split MLL	2	36	7	351
201	IDH2_R172K	Monosomy7	0	4	9	383
202	IDH2_R172K	t(6;9)	0	2	9	385
203	IDH2_R172K	Trisomy 8	0	15	9	372
204	IDH2_R172K	AML1ETO	0	1	9	386
205	TET2	ASXL1	4	6	29	351
206	TET2	FLT3	12	134	21	225
207	TET2	NPM1	10	106	23	253
208	TET2	PHF6	2	7	31	348
209	TET2	KIT	1	22	32	337
210	TET2	CEBPa	2	31	30	325
211	TET2	WT1	3	27	30	326
212	TET2	KRAS	0	8	33	349
213	TET2	NRAS	4	34	29	325
214	TET2	TP53	1	7	32	344
215	TET2	PTEN	1	5	32	353
216	TET2	RUNX1	3	15	29	330
217	TET2	CBF	4	67	29	292
218	TET2	del5q	0	6	33	353
219	TET2	EVI1pos	1	4	32	355
220	TET2	MLLPTD or split MLLPTD	0	18	33	341
221	TET2	splitMLLPTD or split MLL	1	21	32	338
222	TET2	MLLPTD or split MLL	1	37	32	322
223	TET2	Monosomy7	1	2	32	357
224	TET2	t(6;9)	0	2	33	357
225	TET2	Trisomy 8	1	14	32	345
226	TET2	AML1ETO	0	1	33	358
227	ASXL1	FLT3	0	146	10	239

228	ASXL1	NPM1	1	117	9	268
229	ASXL1	PHF6	1	8	9	373
230	ASXL1	KIT	0	22	10	363
231	ASXL1	CEBPa	2	32	8	349
232	ASXL1	WT1	0	30	10	349
233	ASXL1	KRAS	0	8	10	375
234	ASXL1	NRAS	1	38	9	346
235	ASXL1	TP53	0	8	9	370
236	ASXL1	PTEN	0	6	10	378
237	ASXL1	RUNX1	5	15	4	356
238	ASXL1	CBF	0	71	10	314
239	ASXL1	del5q	0	6	10	379
240	ASXL1	EVI1pos	0	5	10	380
241	ASXL1	MLLPTD or split MLLPTD	0	17	10	368
242	ASXL1	splitMLLPTD or split MLL	0	22	10	363
243	ASXL1	MLLPTD or split MLL	0	37	10	348
244	ASXL1	Monosomy7	0	4	10	381
245	ASXL1	t(6;9)	0	2	10	383
246	ASXL1	Trisomy 8	0	15	10	370
247	ASXL1	AML1ETO	0	1	10	384
248	FLT3	NPM1	63	55	84	195
249	FLT3	PHF6	3	6	143	241
250	FLT3	KIT	0	23	147	227
251	FLT3	CEBPa	13	21	131	228
252	FLT3	WT1	18	12	127	234
253	FLT3	KRAS	1	7	146	241
254	FLT3	NRAS	3	37	144	212
255	FLT3	TP53	1	7	144	237
256	FLT3	PTEN	2	4	144	246
257	FLT3	RUNX1	6	14	139	223
258	FLT3	CBF	6	66	141	184
259	FLT3	del5q	1	5	146	245
260	FLT3	EVI1pos	1	4	146	246
261	FLT3	MLLPTD or split MLLPTD	10	8	137	242
262	FLT3	splitMLLPTD or split MLL	2	20	145	230
263	FLT3	MLLPTD or split MLL	11	27	136	223
264	FLT3	Monosomy7	0	4	147	246

265	FLT3	t(6;9)	1	1	146	249
266	FLT3	Trisomy 8	9	6	138	244
267	FLT3	AML1ETO	0	1	147	249
268	NPM1	PHF6	0	9	118	266
269	NPM1	KIT	2	21	116	258
270	NPM1	CEBPa	3	31	113	246
271	NPM1	WT1	6	24	111	250
272	NPM1	KRAS	3	5	115	272
273	NPM1	NRAS	14	26	103	253
274	NPM1	TP53	1	7	115	266
275	NPM1	PTEN	3	3	115	275
276	NPM1	RUNX1	4	16	114	248
277	NPM1	CBF	0	72	118	207
278	NPM1	del5q	0	6	118	273
279	NPM1	EVI1pos	0	5	118	274
280	NPM1	MLLPTD or split MLLPTD	0	18	118	261
281	NPM1	splitMLLPTD or split MLL	0	22	118	257
282	NPM1	MLLPTD or split MLL	0	38	118	241
283	NPM1	Monosomy7	0	4	118	275
284	NPM1	t(6;9)	0	2	118	277
285	NPM1	Trisomy 8	2	13	116	266
286	NPM1	AML1ETO	0	1	118	278
287	PHF6	KIT	0	23	9	361
288	PHF6	CEBPa	2	32	7	348
289	PHF6	WT1	0	30	9	348
290	PHF6	KRAS	0	8	9	374
291	PHF6	NRAS	0	39	9	344
292	PHF6	TP53	0	8	9	368
293	PHF6	PTEN	0	6	9	377
294	PHF6	RUNX1	1	19	8	350
295	PHF6	CBF	1	70	8	314
296	PHF6	del5q	1	5	8	379
297	PHF6	EVI1pos	1	4	8	380
298	PHF6	MLLPTD or split MLLPTD	1	17	8	367
299	PHF6	splitMLLPTD or split MLL	0	22	9	362
300	PHF6	MLLPTD or split MLL	1	37	8	347
301	PHF6	Monosomy7	0	4	9	380

302	PHF6	t(6;9)	0	2	9	382
303	PHF6	Trisomy 8	1	13	8	371
304	PHF6	AML1ETO	0	1	9	383
305	KIT	CEBPa	2	32	21	338
306	KIT	WT1	0	30	22	339
307	KIT	KRAS	0	8	22	365
308	KIT	NRAS	2	38	21	335
309	KIT	TP53	0	8	23	358
310	KIT	PTEN	0	6	23	367
311	KIT	RUNX1	0	20	22	340
312	KIT	CBF	21	51	2	323
313	KIT	del5q	0	6	23	368
314	KIT	EVI1pos	0	5	23	369
315	KIT	MLLPTD or split MLLPTD	0	18	23	356
316	KIT	splitMLLPTD or split MLL	0	22	23	352
317	KIT	MLLPTD or split MLL	0	38	23	336
318	KIT	Monosomy7	0	4	23	370
319	KIT	t(6;9)	0	2	23	372
320	KIT	Trisomy 8	0	15	23	359
321	KIT	AML1ETO	0	1	23	373
322	CEBPa	WT1	4	26	28	329
323	CEBPa	KRAS	0	8	34	349
324	CEBPa	NRAS	2	38	32	320
325	CEBPa	TP53	0	8	34	343
326	CEBPa	PTEN	0	6	34	352
327	CEBPa	RUNX1	0	20	33	326
328	CEBPa	CBF	4	68	30	291
329	CEBPa	del5q	0	6	34	353
330	CEBPa	EVI1pos	1	4	33	355
331	CEBPa	MLLPTD or split MLLPTD	2	16	32	343
332	CEBPa	splitMLLPTD or split MLL	0	21	34	338
333	CEBPa	MLLPTD or split MLL	2	35	32	324
334	CEBPa	Monosomy7	0	3	34	356
335	CEBPa	t(6;9)	0	2	34	357
336	CEBPa	Trisomy 8	1	14	33	345
337	CEBPa	AML1ETO	0	1	34	358
338	WT1	KRAS	0	8	30	351

339	WT1	NRAS	3	37	27	323
340	WT1	TP53	0	8	30	345
341	WT1	PTEN	0	6	30	354
342	WT1	RUNX1	3	17	26	330
343	WT1	CBF	1	69	29	292
344	WT1	del5q	0	6	30	355
345	WT1	EVI1pos	0	4	30	357
346	WT1	MLLPTD or split MLLPTD	2	16	28	345
347	WT1	splitMLLPTD or split MLL	0	22	30	339
348	WT1	MLLPTD or split MLL	2	36	28	325
349	WT1	Monosomy7	0	4	30	357
350	WT1	t(6;9)	1	1	29	360
351	WT1	Trisomy 8	1	14	29	347
352	WT1	AML1ETO	0	1	30	360
353	KRAS	NRAS	0	40	8	346
354	KRAS	TP53	0	8	8	371
355	KRAS	PTEN	0	6	8	380
356	KRAS	RUNX1	1	19	7	353
357	KRAS	CBF	2	68	6	319
358	KRAS	del5q	0	6	8	381
359	KRAS	EVI1pos	0	5	8	382
360	KRAS	MLLPTD or split MLLPTD	0	18	8	369
361	KRAS	splitMLLPTD or split MLL	1	21	7	366
362	KRAS	MLLPTD or split MLL	1	37	7	350
363	KRAS	Monosomy7	0	4	8	383
364	KRAS	t(6;9)	0	2	8	385
365	KRAS	Trisomy 8	0	15	8	372
366	KRAS	AML1ETO	0	1	8	386
367	NRAS	TP53	0	8	39	341
368	NRAS	PTEN	2	4	38	351
369	NRAS	RUNX1	2	18	35	326
370	NRAS	CBF	12	60	28	296
371	NRAS	del5q	0	6	40	350
372	NRAS	EVI1pos	1	4	39	352
373	NRAS	MLLPTD or split MLLPTD	0	18	40	338
374	NRAS	splitMLLPTD or split MLL	2	20	38	336

375	NRAS	MLLPTD or split MLL	2	36	38	320
376	NRAS	Monosomy7	0	4	40	352
377	NRAS	t(6;9)	0	2	40	354
378	NRAS	Trisomy 8	0	15	40	341
379	NRAS	AML1ETO	0	1	40	355
380	TP53	PTEN	1	5	7	375
381	TP53	RUNX1	1	19	7	348
382	TP53	CBF	0	72	8	309
383	TP53	del5q	1	5	7	376
384	TP53	EVI1pos	0	5	8	376
385	TP53	MLLPTD or split MLLPTD	0	17	8	364
386	TP53	splitMLLPTD or split MLL	0	22	8	359
387	TP53	MLLPTD or split MLL	0	37	8	344
388	TP53	Monosomy7	0	4	8	377
389	TP53	t(6;9)	0	2	8	379
390	TP53	trisomy 8	0	15	8	366
391	TP53	AML1ETO	0	1	8	380
392	PTEN	RUNX1	0	20	6	355
393	PTEN	CBF	1	71	5	319
394	PTEN	del5q	0	6	6	384
395	PTEN	EVI1pos	0	5	6	385
396	PTEN	MLLPTD or split MLLPTD	0	18	6	372
397	PTEN	splitMLLPTD or split MLL	0	22	6	368
398	PTEN	MLLPTD or split MLL	0	38	6	352
399	PTEN	Monosomy7	0	4	6	386
400	PTEN	t(6;9)	0	2	6	388
401	PTEN	trisomy 8	0	15	6	375
402	PTEN	AML1ETO	0	1	6	389
403	RUNX1	CBF	2	66	18	296
404	RUNX1	del5q	3	3	17	359
405	RUNX1	EVI1pos	0	4	20	358
406	RUNX1	MLLPTD or split MLLPTD	3	15	17	347
407	RUNX1	splitMLLPTD or split MLL	0	19	20	343
408	RUNX1	MLLPTD or split MLL	3	32	17	330
409	RUNX1	Monosomy7	1	2	19	360

410	RUNX1	t(6;9)	0	2	20	360
411	RUNX1	trisomy 8	0	14	20	348
412	RUNX1	AML1ETO	0	1	20	361
413	CBF	del5q	0	6	72	319
414	CBF	EVI1pos	0	5	72	320
415	CBF	MLLPTD or split MLLPTD	0	18	72	307
416	CBF	splitMLLPTD or split MLL	0	22	72	303
417	CBF	MLLPTD or split MLL	0	38	72	287
418	CBF	Monosomy7	0	4	72	321
419	CBF	t(6;9)	0	2	72	323
420	CBF	trisomy 8	0	15	72	310
421	CBF	AML1ETO	1	0	71	325
422	del5q	EVI1pos	0	5	6	386
423	del5q	MLLPTD or split MLLPTD	0	18	6	373
424	del5q	splitMLLPTD or split MLL	0	22	6	369
425	del5q	MLLPTD or split MLL	0	38	6	353
426	del5q	Monosomy7	0	4	6	387
427	del5q	t(6;9)	0	2	6	389
428	del5q	trisomy 8	0	15	6	376
429	del5q	AML1ETO	0	1	6	390
430	EVI1pos	MLLPTD or split MLLPTD	0	18	5	374
431	EVI1pos	splitMLLPTD or split MLL	0	22	5	370
432	EVI1pos	MLLPTD or split MLL	0	38	5	354
433	EVI1pos	Monosomy7	0	4	5	388
434	EVI1pos	t(6;9)	0	2	5	390
435	EVI1pos	trisomy 8	0	15	5	377
436	EVI1pos	AML1ETO	0	1	5	391
437	MLLPTD or split MLLPTD	Monosomy7	1	3	17	376
438	MLLPTD or split MLLPTD	t(6;9)	0	2	18	377
439	MLLPTD or split MLLPTD	trisomy 8	0	15	18	364
440	MLLPTD or split MLLPTD	AML1ETO	0	1	18	378
441	splitMLLPTD or split MLL	Monosomy7	0	4	22	371

442	splitMLLPTD or split MLL	t(6;9)	0	2	22	373
443	splitMLLPTD or split MLL	trisomy 8	0	15	22	360
444	splitMLLPTD or split MLL	AML1ETO	0	1	22	374
445	MLLPTD or split MLL	Monosomy7	1	3	37	356
446	MLLPTD or split MLL	t(6;9)	0	2	38	357
447	MLLPTD or split MLL	trisomy 8	0	15	38	344
448	MLLPTD or split MLL	AML1ETO	0	1	38	358
449	Monosomy7	t(6;9)	0	2	4	391
450	Monosomy7	trisomy 8	0	15	4	378
451	Monosomy7	AML1ETO	0	1	4	392
452	t(6;9)	trisomy 8	0	15	2	380
453	t(6;9)	AML1ETO	0	1	2	394
454	Trisomy 8	AML1ETO	0	1	15	381

1) Single nucleotide variants which could not be verified as bona fide somatic mutations were censored from analysis, therefore sample number does not add up to 398 in all instances.
2) Number of patients mutated for both gene #1 and gene #2.
3) Number of patients wildtype for gene #1 but mutant for gene #2.
4) Number of patients mutated for gene #1 and wildtype for gene #2.
5) Number of patients wildtype for both genes.

Table S7. Frequently co-occurring genetic abnormalities[1].

Mutated Gene #1	Mutated Gene #2	M/M[2]	WT/M[3]	% M/M[4]	M/WT[5]	WT/WT[6]	% M/WT[7]	p-value[8]	Adjusted p-value[9]
ASXL1	RUNX1	5	15	25.0	4	356	1.1	<0.001	<0.001
DNMT3A	NPM1	57	57	50.0	32	239	11.8	<0.001	<0.001
DNMT3A	FLT3 ITD	52	92	36.1	37	204	15.4	<0.001	<0.001
DNMT3A	IDH1	13	9	59.1	76	286	21.0	<0.001	0.008
DNMT3A	IDH1 or IDH2	19	32	37.3	70	262	21.1	0.02	0.91
FLT3 ITD	NPM1	63	55	53.4	84	195	30.1	<0.001	<0.001
FLT3 ITD	WT1	18	12	60.0	127	234	35.2	0.01	0.94
IDH1 or IDH2	NPM1	31	87	26.3	26	251	9.4	<0.001	0.002
IDH1	NPM1	14	104	11.9	10	268	3.6	0.004	0.38
IDH1	PTEN	2	4	33.3	22	367	5.7	0.05	0.69
IDH2	NPM1	17	101	14.4	16	262	5.8	0.01	0.67
IDH2 R140Q	NPM1	16	102	13.6	8	270	2.9	<0.001	0.01
KIT	CBF	21	51	29.2	2	323	0.6	<0.001	<0.001
NRAS	CBF	12	60	16.7	28	296	8.6	0.05	0.1
RUNX1	Del 5q	3	3	50.0	17	359	4.5	0.002	1.0
TET2	ASXL1	4	6	40.0	29	351	7.6	0.006	0.03

1) Single nucleotide variants which could not be verified as bona fide somatic mutations were censored from analysis, therefore sample number does not sum up to 398 in all instances.
2) Number of patients mutated for both gene #1 and gene #2.
3) Number of patients wildtype for gene #1 but mutant for gene #2.
4) Percentage of patients mutant for gene #1 and gene #2 over all patients mutated for either gene.
5) Number of patients mutated for gene #1 and wildtype for gene #2.
6) Number of patients wildtype for both genes.
7) Percentage of patients mutant for either gene over all patients wildtype for either gene.
8) P-value by Fisher's exact test.
9) P-value adjusted for multiple comparisons.

Table S8. Mutually exclusive genetic abnormalities[1].

Mutated Gene #1	Mutated Gene #2	M/M[2]	WT/M[3]	% M/M[4]	M/WT[5]	WT/WT[6]	% M/WT[7]	p-value[8]	Adjusted p-value[9]
ASXL1	FLT3	0	146	0	10	239	4.0	0.02	0.94
CBF	MLL abnormalities	0	38	0	72	287	20.1	<0.001	0.99
CBF	Split MLL	0	22	0	72	303	19.2	0.02	1.0
CBF	MLL PTD	0	18	0	72	307	19.0	0.05	1.0
DNMT3A	CBF	1	71	1.4	88	225	28.1	<0.001	0.11
DNMT3A	Splt MLL	1	21	4.6	88	275	24.2	0.04	0.97
DNMT3A R882	WT1	0	29	0	63	287	18.0	0.01	0.92
FLT3	CBF	6	66	8.3	141	184	43.4	<0.001	0.02
FLT3	NRAS	3	37	7.5	144	212	40.5	<0.001	0.008
FLT3	KIT	0	23	0	147	227	39.3	<0.001	0.04
FLT3	Splt MLL	2	20	9.1	145	230	38.7	0.005	0.39
IDH1 or IDH2	CBF	1	71	1.4	56	267	17.3	<0.001	0.63
IDH1 or IDH2	TET2	0	33	0	56	301	15.7	0.008	0.97
IDH1 or IDH2	WT1	0	30	0	56	303	15.6	0.01	0.98
IDH1 or IDH2	FLT3	13	133	8.9	44	205	17.7	0.02	1.0
IDH1 or IDH2	CEBPA	1	33	2.9	56	302	15.6	0.04	0.99
IDH1	FLT3	4	142	2.7	20	230	8.0	0.04	1.0
IDH2	CBF	0	72	0	33	291	10.2	0.002	0.99
NPM1	CBF	0	72	0	118	207	36.3	<0.001	0.001
NPM1	MLL abnormalities	0	38	0	118	241	32.9	<0.001	0.02
NPM1	Split MLL	0	22	0	118	257	31.5	<0.001	0.59
NPM1	MLL PTD	0	18	0	118	261	31.1	0.002	0.59
NPM1	CEBPA	3	31	8.2	113	246	31.5	0.005	0.34
NPM1	KIT	2	21	8.7	116	258	31.0	0.03	0.99
WT1	CBF	1	69	1.4	29	292	9.0	0.03	1.0

1) Single nucleotide variants which could not be verified as bona fide somatic mutations were censored from analysis, therefore sample number does not sum up to 398 in all instances.
2) Number of patients mutated for both gene #1 and gene #2
3) Number of patients wildtype for gene #1 but mutant for gene #2
4) Percentage of patients mutant for gene #1 and gene #2 over all patients mutated for either gene
5) Number of patients mutated for gene #1 and wildtype for gene #2
6) Number of patients wildtype for both genes
7) Percentage of patients mutant for either genes over all patients wildtype for either gene
8) P-value by Fisher's exact test.
9) P-value adjusted for multiple comparisons

Table S9. Univariate analysis of the effects of mutations in individual genes on overall survival in the ECOG E1900 test cohort.[1]

Gene/Cytogenetic Abnormality	Mutational Status	Number of patients	Median Survival (months)	UV analysis p-value[2]	MV analysis p-value[3]
DNMT3A	Mutant	88	14.1	0.19	0.29
	Wildtype	296	21.3		
DNMT3A	R882 Mutant	63	14.1	0.14	0.26
	Wildtype	321	21.3		
DNMT3A	Non-R882 Mutant	27	18.2	0.90	0.91
	Wildtype	357	18.0		
IDH1/2	Mutant for IDH1 or IDH2	56	42.4	0.009	0.001
	Wildtype	358	16.2		
IDH1	Mutant	23	38.7	0.42	0.59
	Wildtype	372	17.0		
IDH2	Mutant	33	49.4	0.01	0.001
	Wildtype	362	16.3		
IDH2	R140Q Mutant	24	-	0.009	0.001
	Wildtype	371	16.6		
IDH2	R172K Mutant	9	41.3	0.58	0.46
	Wildtype	386	16.9		
TET2	Mutant	33	13.2	0.16	0.61
	Wildtype	358	18.0		
ASXL1	Mutant	10	10.3	0.05	0.22
	Wildtype	384	17.7		
FLT3	Mutant	148	13.8	0.006	0.003
	Wildtype	248	22.0		
NPM1	Mutant	118	22.3	0.07	0.005
	Wildtype	278	16.5		
PHF6	Mutant	9	4.3	0.006	0.08
	Wildtype	383	17.7		
KIT	Mutant	23	57.9	0.08	0.6
	Wildtype	373	16.6		
CEBPa	Mutant	34	31.7	0.05	0.03
	Wildtype	358	16.9		
WT1	Mutant	30	12.2	0.23	0.19
	Wildtype	360	17.7		
KRAS	Mutant	8	-	0.17	0.19
	Wildtype	386	16.9		
NRAS	Mutant	40	21.3	0.13	0.19
	Wildtype	355	16.9		

TP53	Mutant	8	12.4	0.14	0.83
	Wildtype	380	18.2		
PTEN	Mutant	6	15.2	0.68	0.68
	Wildtype	389	17.9		
RUNX1	Mutant	20	16.9	0.90	0.63
	Wildtype	361	16.9		
CBF translocations	Present	43	-	0.001	0.47
	Absent	353	16.2		
Del 5q	Present	12	7.0	0.001	0.46
	Absent	384	18.0		
EVI positive	Present	8	2.8	<0.001	0.02
	Absent	388	18.0		
MLL PTD	Present	19	12.6	0.009	0.19
	Absent	377	18.0		
Split MLL	Present	25	11.7	0.05	0.44
	Absent	371	18.2		
Any MLL abnormalities	Present	39	10.9	<0.001	0.33
	Absent	357	19.7		
Monosomy 7	Present	9	3.5	<0.001	0.18
	Absent	387	18.0		
t(6;9)	Present	2	15.8	0.42	0.81
	Absent	394	17.5		
Trisomy 8	Present	19	10.2	0.06	0.03
	Absent	377	18.0		
t(8;21)	Present	29	47.1	0.02	0.37
	Absent	367	16.5		

1) Absence of value under column for overall survival indicates that deaths were not observed.
2) Univariate (UV) analysis p-value (calculated by Log-rank test).
3) Multivariate (MV) analysis p-value taking into account WBC count, age, transplantation, and cytogenetics.

Table S10. Univariate analysis of mutations in individual genes on intermediate-risk group in the ECOG E1900 cohort.[1]

Gene/Cytogenetic Abnormality	Mutational Status	Number of patients	Median Survival (months)	p-value[2]
DNMT3A	Mutant	75	14.08	0.17
	Wildtype	151	22.83	
DNMT3A	R882 Mutant	56	14.08	0.07
	Wildtype	170	22.83	
DNMT3A	Non-R882 Mutant	21	23.52	0.57
	Wildtype	205	17.96	
IDH1/2	Mutant for IDH1 or IDH2	46	-	0.001
	Wildtype	188	15.53	
IDH1	Mutant	21	38.65	0.49
	Wildtype	213	17.53	
IDH2	Mutant	25	-	0.001
	Wildtype	209	16.15	
IDH2	R140Q Mutant	18	-	0.001
	Wildtype	216	16.91	
IDH2	R172K Mutant	7	37.96	0.44
	Wildtype	227	16.94	
TET2	Mutant	17	8.82	0.008
	Wildtype	214	19.08	
ASXL1	Mutant	6	24.42	0.48
	Wildtype	227	17.66	
FLT3	Mutant	120	13.52	0.001
	Wildtype	114	34.31	
NPM1	Mutant	110	23.52	0.04
	Wildtype	124	16.15	
PHF6	Mutant	3	2.53	<0.0001
	Wildtype	229	17.96	
KIT	Mutant	2	-	0.98
	Wildtype	232	17.66	
CEBPa	Mutant	26	31.68	0.14
	Wildtype	207	16.91	
WT1	Mutant	26	10.94	0.12
	Wildtype	205	18.26	
KRAS	Mutant	5	-	0.09
	Wildtype	229	17.53	
NRAS	Mutant	20	-	0.10
	Wildtype	213	16.94	
TP53	Mutant	2	-	0.57
	Wildtype	229	17.89	

PTEN	Mutant	4	-	0.99
	Wildtype	229	17.89	
RUNX1	Mutant	13	16.91	0.54
	Wildtype	215	17.89	
EVI positive	Present	2	1.25	<0.0001
	Absent	232	17.89	
MLL PTD	Present	12	16.54	0.04
	Absent	222	18.26	
Split MLL	Present	7	21.71	0.96
	Absent	227	17.77	
Any MLL abnormalitiy	Present	17	16.15	0.08
	Absent	217	18.95	
Trisomy 8	Present	19	10.16	0.04
	Absent	215	18.25	

1) Absence of value under column for overall survival indicates that deaths were not observed.
2) P-value calculated by Log-rank test.

Table S11: Revised AML Risk Stratification Based on Integrated Mutational Analysis (frequency of patients per cytogenetic/mutational risk category in the Test cohort is shown).

<table>
<tr><th>Cytogenetic Classification</th><th colspan="2">Mutations</th><th>Test cohort (% (N))</th><th>Validation cohort (% (N))</th><th>Overall Risk</th></tr>
<tr><td>Inversion (16), t(8;21)</td><td colspan="2">Any</td><td>19.7% (71)</td><td>15.5% (13)</td><td rowspan="2">Favorable</td></tr>
<tr><td rowspan="6">Normal Karyotype or Intermediate Risk Cytogenetic Lesions</td><td>FLT3-ITD negative</td><td>NPM1 and IDH1/2 mutant</td><td>5.8% (21)</td><td>7.1% (6)</td></tr>
<tr><td>FLT3-ITD negative</td><td>ASXL1, MLL-PTD, PHF6 and TET2-wildtype</td><td rowspan="3">35.5% (129)</td><td rowspan="3">27.4% (23)</td><td rowspan="3">Intermediate</td></tr>
<tr><td>FLT3-ITD negative or positive</td><td>CEBPA mutant</td></tr>
<tr><td>FLT3-ITD positive</td><td>MLL-PTD, TET2, and DNMT3A wildtype, and trisomy 8 negative</td></tr>
<tr><td>FLT3-ITD negative</td><td>TET2, MLL-PTD, ASXL1, or PHF6 mutant</td><td rowspan="2">20.9% (76)</td><td rowspan="2">21.4% (18)</td><td rowspan="3">Unfavorable</td></tr>
<tr><td>FLT3-ITD positive</td><td>TET2, MLL-PTD, DNMT3A mutant or trisomy 8</td></tr>
<tr><td>Unfavorable</td><td colspan="2">Any</td><td>18.2% (66)</td><td>28.6% (24)</td></tr>
</table>

Table S12. Genetic prognostic schema is independent of treatment-related mortality[1] and chemotherapy resistance[2] in the test cohort and the entire cohort of the analyzed ECOG E1900 patients.

Test cohort (n=398)			
	Hazard Ratio	Confidence Interval	p-value
Favorable	Reference		<0.001
Intermediate	1.88	1.15 – 3.05	
Unfavorable	6.16	3.83 – 9.88	
Entire cohort (n=502)			
	Hazard Ratio	Confidence Interval	p-value
Favorable	Reference		<0.001
Intermediate	1.83	1.18 – 2.85	
Unfavorable	5.76	3.76 – 8.82	

[1]Treatment-related mortality defined as death within 30 days after beginning induction chemotherapy.
[2]Chemotherapy resistance defined as failure to enter complete remission despite not incurring treatment-related morality, or relapse.

Table S13. Differential response to high-dose versus standard-dose daunorubicin induction chemotherapy based on genotype of AML patients.

Gene/Cytogenetic Abnormality	Mutational Status	p-value[1]	Adjusted p-value[2]
DNMT3A	Mutant	0.01	0.10
	Wildtype	0.14	0.28
IDH1	Mutant	0.62	-
	Wildtype	0.01	-
IDH2	Mutant	0.33	-
	Wildtype	0.05	-
IDH2 R140Q	R140Q Mutant	0.15	1.0
	Wildtype	0.05	0.22
IDH2 R172K	R172K Mutant	0.73	-
	Wildtype	0.02	-
TET2	Mutant	0.45	1.0
	Wildtype	0.006	0.04
ASXL1	Mutant	0.08	0.50
	Wildtype	0.009	0.05
FLT3	Mutant	0.14	0.71
	Wildtype	0.10	0.30
NPM1	Mutant	0.01	0.11
	Wildtype	0.20	0.20
PHF6	Mutant	0.19	0.77
	Wildtype	0.005	0.04
KIT	Mutant	0.12	-
	Wildtype	0.004	-
CEBPa	Mutant	0.56	0.56
	Wildtype	0.003	0.03
WT1	Mutant	0.2	-
	Wildtype	0.02	-
KRAS	Mutant	0.62	-
	Wildtype	0.01	-
NRAS	Mutant	0.15	-
	Wildtype	0.04	-
TP53	Mutant	0.75	-
	Wildtype	0.01	-
PTEN	Mutant	0.78	-
	Wildtype	0.02	-
RUNX1	Mutant	0.47	-
	Wildtype	0,01	-
EVI positive	Present	0.90	-
	Absent	0.03	-
MLL PTD	Present	0.27	-
	Absent	0.01	-

Split MLL	Present	0.007	0.07
	Absent	0.06	0.25

1) P-value calculated by Log-rank test.
2) P-value adjusted for multiple testing by a step-down Holm procedure (see Supplementary Methods). “-“ indicates adjusted p-value not performed.