Clonal hematopoiesis and risk of acute myeloid leukemia

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 doi:10.3324/haematol.2018.215269

Received: January 18, 2019.

Accepted: April 16, 2019.

Pre-published: April 19, 2019.

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Online Supplementary Methods, Figures and Tables

Study Population

Details of the NHS design and methods are published elsewhere[1]. Briefly, the NHS began in 1976 with 121,701 female United States (US) registered nurses age 30 to 55 years who returned an enrollment questionnaire, which queried medical history and a variety of potential health risk factors. The participants have subsequently returned biennial follow-up questionnaires to update risk factor and medical information. The HFPS began in 1986 with 51,529 male US-licensed health professionals age 40-75 years who returned a baseline questionnaire and has utilized similar follow-up methods as for the NHS, including biennial questionnaires[2]. In both cohorts, self-reported diagnoses are confirmed (with participant consent) by review of medical records or via tumor registry linkage, as are diagnoses first identified via death follow-up. To date, a majority of participants in both cohorts have consistently returned the biennial follow-up questionnaires (>90% in most follow-up cycles, and >95% in the blood subcohorts described below).

Biospecimen collections

From 1989-1990, 32,826 women in the NHS provided a heparinized whole blood sample[3]. From 2000-2001, 18,743 women who provided a sample in 1989-1990 provided a second whole blood sample using the same protocol[4]. From 1993-1995, 18,018 men provided an EDTA whole blood sample using similar collection methods to those for the NHS; a second blood collection has not been performed in the HPFS. Participants provided written informed consent at time of blood collection. The present study protocol was approved by the Institutional Review Boards of Brigham and Women's Hospital, the Harvard TH Chan School of Public Health and Washington University (Human Research Protection Office IRB#201607023).

Case definition and control selection

For the present study, we utilized a nested case-control design. Specifically, we ascertained cases from the NHS and HPFS "blood subcohorts," which comprise the subset of cohort members who contributed to the respective first blood collections described above. We included all blood subcohort participants with a confirmed incident diagnosis of AML (ICD-8 or -9 codes of 205.0) that occurred after blood draw in individuals with no prior history of malignancy (except non-melanoma skin cancer). We matched two controls per case among individuals with no history of cancer (other than non-melanoma skin cancer) as of the case's AML diagnosis date (i.e., the "index date"). Matching criteria included cohort (which also achieved matching by sex), race (White, African-American, Asian, other), date of birth (± 1 year), date (± 1 year) and time of day of blood draw (± 4 hours) and fasting status (<8, 8+ hours) at blood draw. For the NHS cases with a second blood collection sample, we matched among controls with a second blood sample using the same matching criteria as for first blood samples.

These protocols selected 35 cases (16 NHS, 19 HPFS) and 70 controls (32 NHS, 38 HPFS), including 12 cases and 24 controls in the NHS with two blood samples, for a total of 141 samples. After exclusion of four samples with insufficient volume, 137 samples were shipped to Washington University for ECS testing. The laboratory technician was blinded to sample case-control status but could identify specimens from the same matched set and repeat samples from the same individual, to ensure that matched set trios of samples were tested together, and to facilitate ECS protocols.

CHIP determination and validation

Library preparation. Sequencing libraries were prepared as previously described[5]. As for previous studies, the Illumina TruSight Myeloid Sequencing Panel was used for targeted capture from all or part of 54 leukemia-associated genes (Supplementary Table 1). Library concentration and quality was assessed on the Agilent

2200 TapeStation and libraries were pooled into equimolar groups of six. The pooled libraries were again quantified on the TapeStation and submitted for sequencing.

Sequencing. Each pool of six individual libraries was sequenced on individual lanes of the Illumina HiSeq 3000 platform using a 300-cycle kit as specified by the manufacturer. A separate technical replicate ECS library was independently generated and sequenced from each sample to reduce false positives. Technical replicates were always sequenced on different machine runs to avoid run-specific artifacts. Approximately 5-10% of PhiX control DNA was spiked into each sequencing experiment. Each lane of the HiSeq 3000 run contained approximately 300M paired-end 146 bp reads with corresponding 16 bp unique molecular index (UMI) and 8 bp sample-specific index sequences. Sequenced reads were demultiplexed by sample-specific index allowing for at most one mismatch in the index sequence. Raw sequence reads were aligned using Bowtie 2 [6] as previously described[5].

Error Corrected Sequencing Analysis. ECS analysis of raw sequencing results was performed as previously described[5] with the exception of one modification described below. Germline variants identified by the 1000 Genomes Project (Aug 2015 release)[7] above 0.001 minor allele fraction were excluded from analysis. Likely clonal single nucleotide variants (SNV) at <0.4 VAF were reported and annotated using Annovar[8] with COSMIC version 77 [9], Ensembl version 75 (Feb 2014 release)[10], and 1000 Genomes (Aug 2015 release)[7] databases. The amino acid substitutions were predicted based on the canonical transcript reported in COSMIC. We reported SNVs identified in both technical replicates for a given sample.

Insertions and deletions (indel) were called using VarScan2 [11] as described previously[5]. Single nucleotide indels in homopolymer tracks of ≥4 nucleotides in length and occurring in repetitive elements were filtered out of the final analysis. Clonal indels (<0.4 VAF) detected in both technical replicates from a given sample were reported and annotated using Annovar [8] as described previously for rare clonal SNVs.

The only modification we made to the previously published ECS analytic approach[5] addressed the limitation that the previous approach was underpowered to detect multiple clonal SNVs co-occurring at the same position because multiple true-positives could artificially inflate the calculated position-specific error rate. This prevented the identification of rare clonal mutations above the true background error rate at that position, but below/near the estimated error rate calculated based on other co-occurring clonal SNVs at higher VAFs, resulting in false negatives at frequently mutated “hot spot” loci[5]. In the present study, to improve rare SNV identification at potential hot spots, we re-called variants from the binomial error model after removing the specific variants identified in the first iteration of analysis until a subsequent iteration revealed no additional new variants.

Droplet Digital PCR Analysis. To validate our ECS-based variant calls, we performed droplet digital PCR (ddPCR) for 61-point mutations (n=41) and indels (n=20). Droplets were generated and assayed on the QX200 droplet generator and reader (Bio-Rad), respectively, using the standard protocol[12]. All probes were designed by Bio-Rad based on MIQE guidelines for quantitative digital PCR[13]. The VAF was estimated from droplets lacking the reference allele and the Poisson-estimated number of singleton droplets as described previously [5,14].

Statistical Analysis

We classified participants as “positive” for a mutation if that mutation was identified by ECS in both technical replicates from one participant sample. For women with repeat blood samples in the study we also identified mutations that were present (positive) only in the second blood sample and/or in both. We combined the data from the NHS and HPFS to maximize statistical power for analysis. For mutations that were present (positive) in ≥4 participants and for selected VAF thresholds (≥0.001, ≥0.005, ≥0.01 and ≥0.02), we used conditional logistic regression, conditioning on the matched sets, to calculate odds ratios (OR) and 95% confidence intervals (CI) to estimate the relative risk of AML for detection of a given variant or VAF threshold. We analyzed two series of variables, including one in which we defined mutation status according to the variants detected in the first blood collection samples, and another series in which we defined mutation status according to variants detected in either the first or the second blood collection samples. In all models we treated the respective variant-negative group as the reference category. Sparse data precluded the evaluation of potential

confounding by other AML risk factors—such as body mass index (BMI) or smoking history[15,16]—or of heterogeneity of mutation-AML risk associations by follow-up time interval or other potential effect modifiers (such as sex, BMI or smoking history). In exploratory analyses restricted to AML cases, we generated Kaplan-Meier plots to compare time (months) to AML diagnosis for individuals with and without selected pre-diagnosis mutations and VAF thresholds. We also investigated whether clone size (specifically, the size of the most common clone at each collection) or clonal expansion over time (i.e., the largest increase in VAF, regardless of the corresponding variant, for women with two blood samples) was correlated with time to AML diagnosis, using Spearman partial correlations adjusted for age and (in relation to clone size at collection one) sex. Lastly, we conducted a sensitivity analysis omitting the few individuals with a follow-up interval of less than one year after the first blood draw (Table 1) to assess their influence on the main findings. All statistical analyses were performed with SAS version 9.3; graphical descriptive analyses were performed with R version 3.3.3 using the ggplot2 and ppcor packages[17]. All hypothesis tests were two-tailed and assumed an α-error of 0.05.

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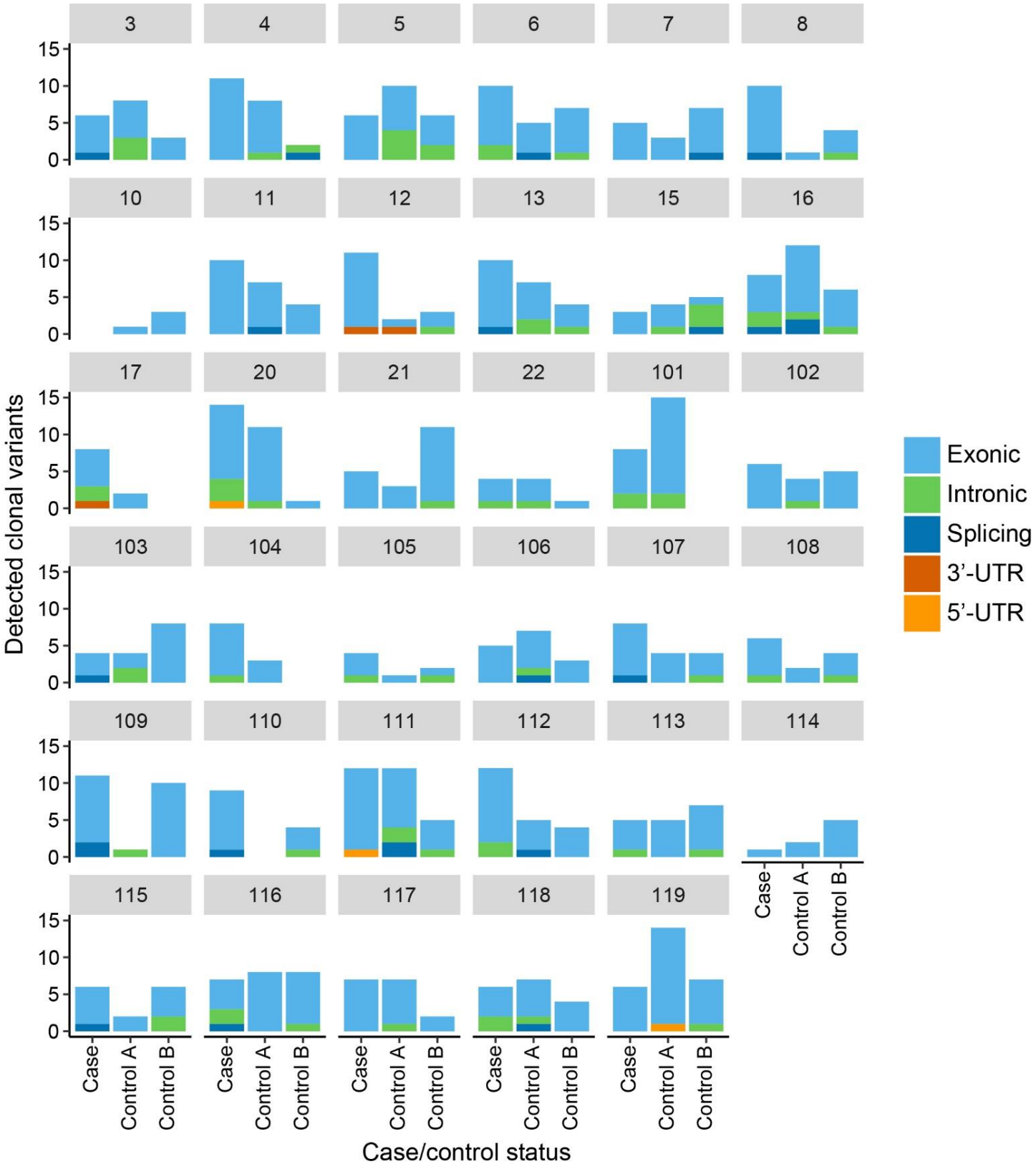
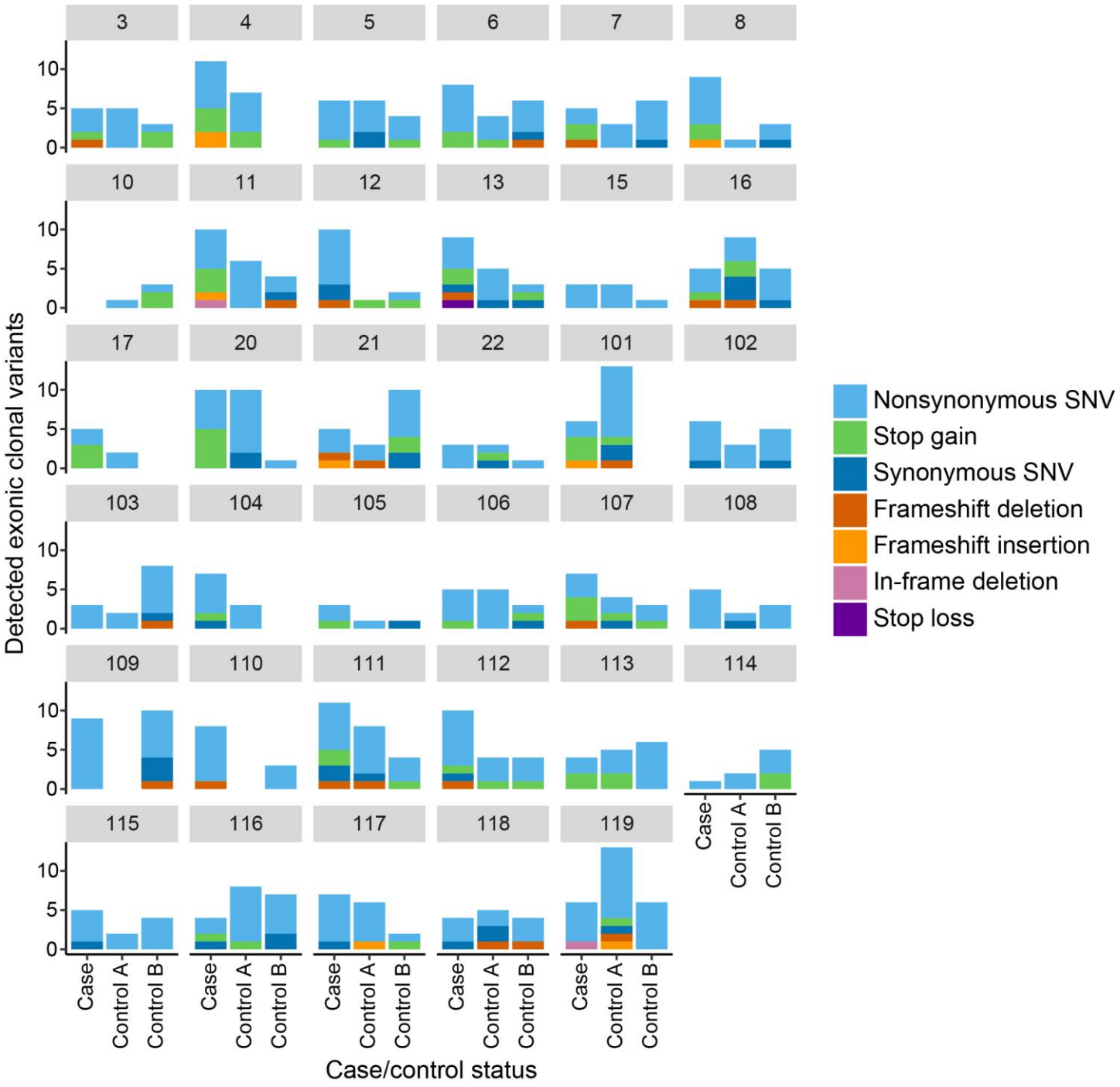
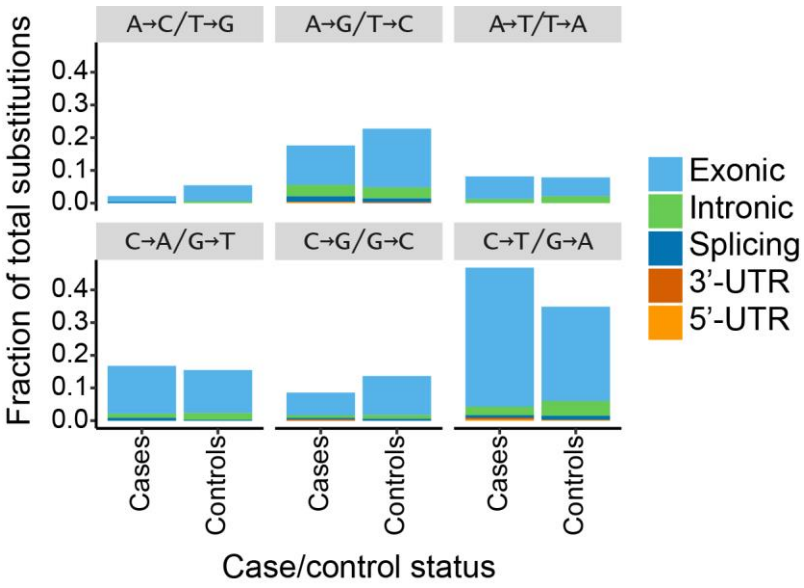
Supplementary Figure 1A. The total number of mutations found per individual, color coded by annotation. Each panel depicts a matched trio of one case and two controls. Trios with set numbers <100 are women in the Nurses' Health Study and trios numbered >100 are men in the Health Professionals Follow-up Study.



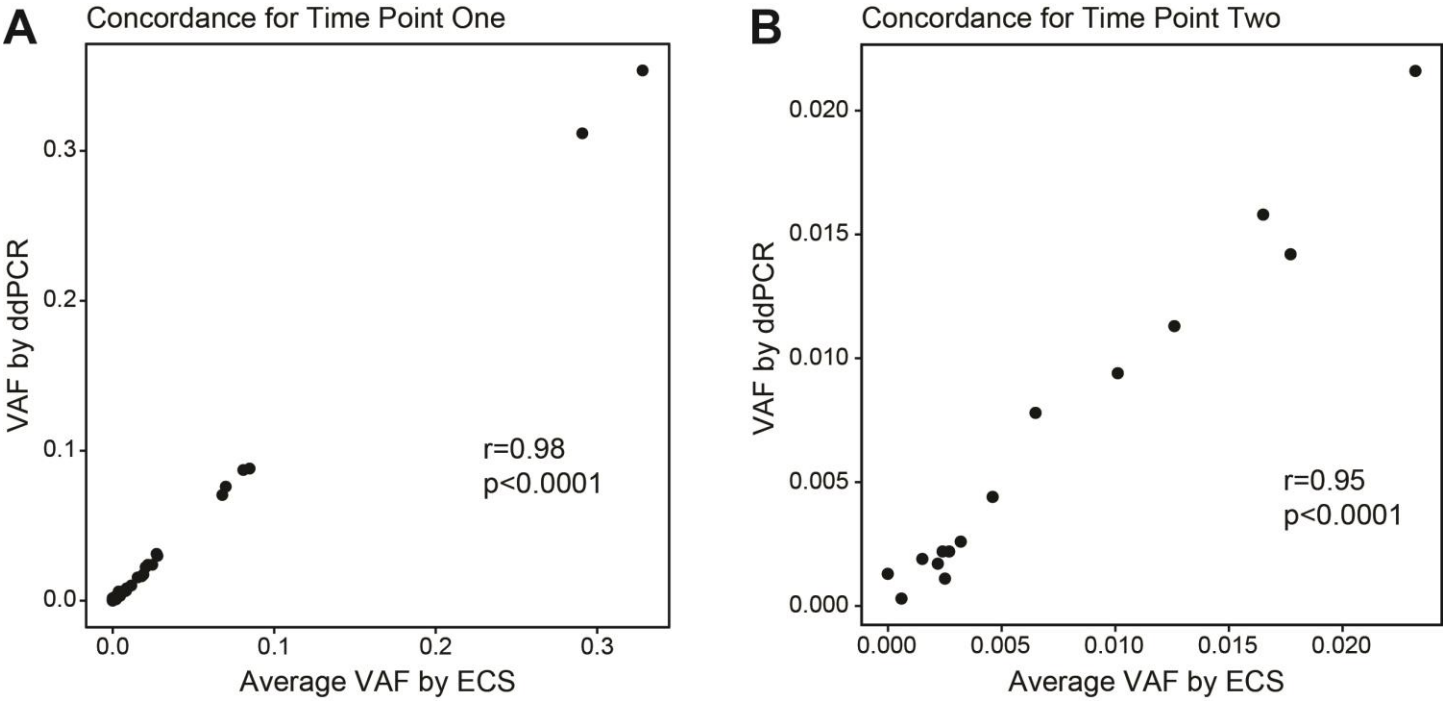
Supplementary Figure 1B. The total number of coding mutations found per individual. Each panel depicts a matched trio of one case and two controls. Trios with a set number <100 are women in the Nurses' Health Study; those with a set number >100 are men in the Health Professionals Follow-up Study.



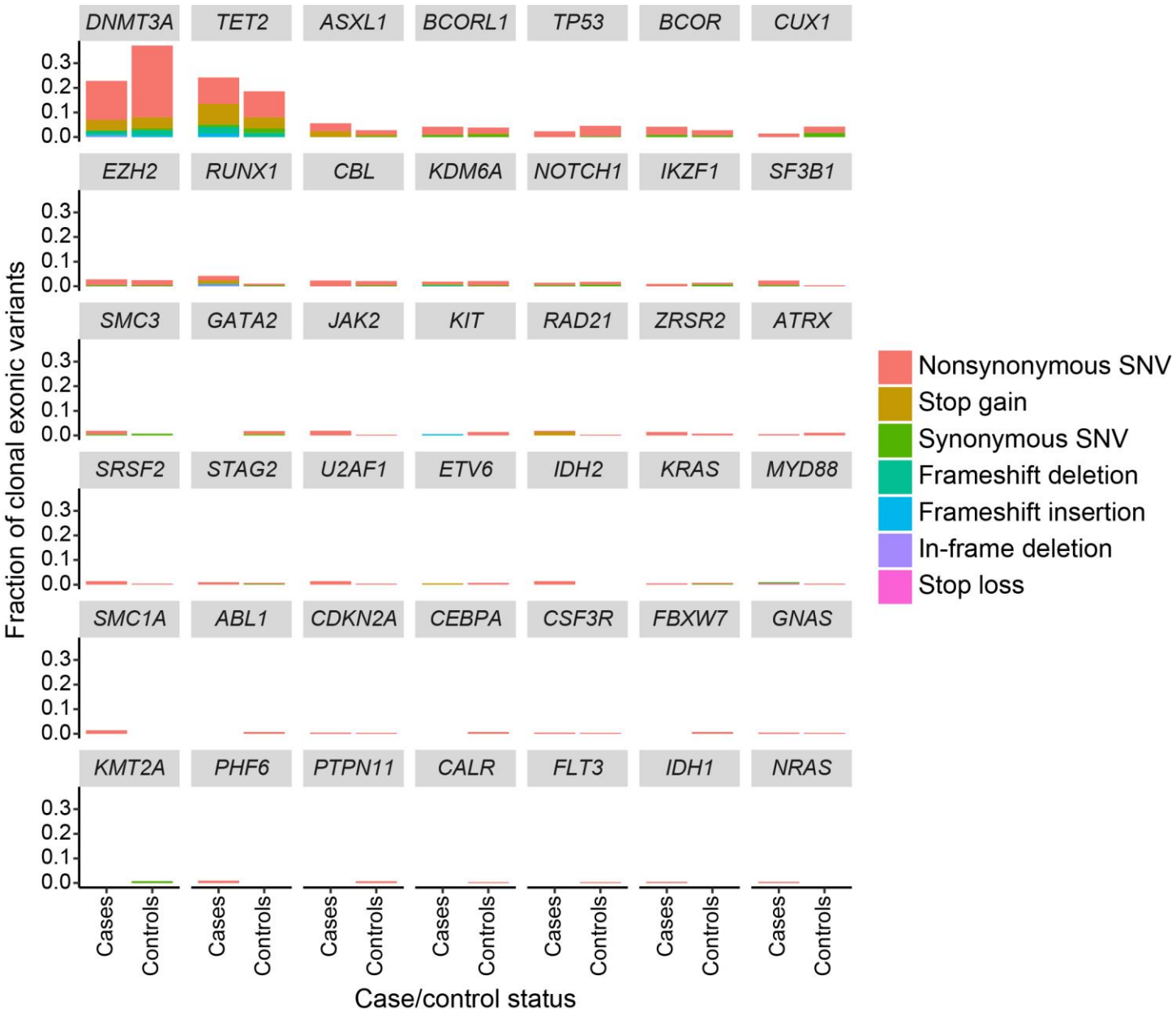
Supplementary Figure 1C. The proportion of specific point mutations observed in cases and controls across all matched case-control trios in the study sample, color coded by annotation.



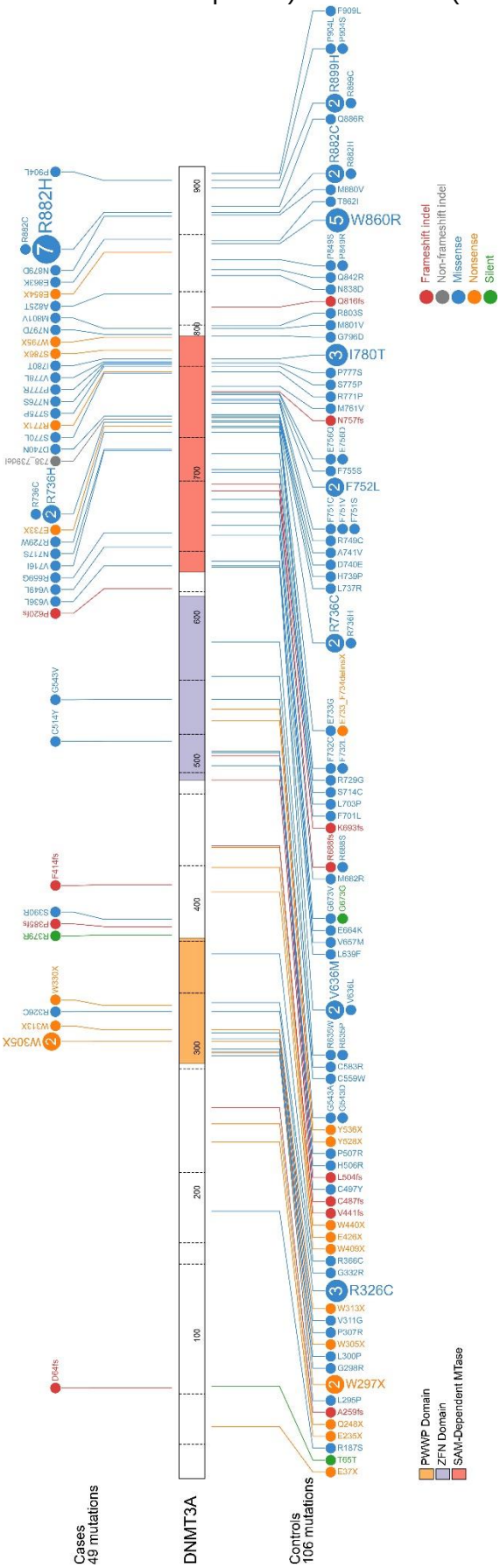
Supplementary Figure 2. Plots and Spearman rank correlation coefficients showing a high correspondence of variant allele fraction (VAF) calls by error-corrected sequencing (ECS) and droplet digital PCR (ddPCR). Each data point represents the average VAF observed by ECS (of two technical replicates) compared to the VAF observed by ddPCR. Panel A shows the concordance of variant calls for samples from the first blood collection (n=46). Panel B shows the concordance of variant calls for samples from the second blood collection (n=15).



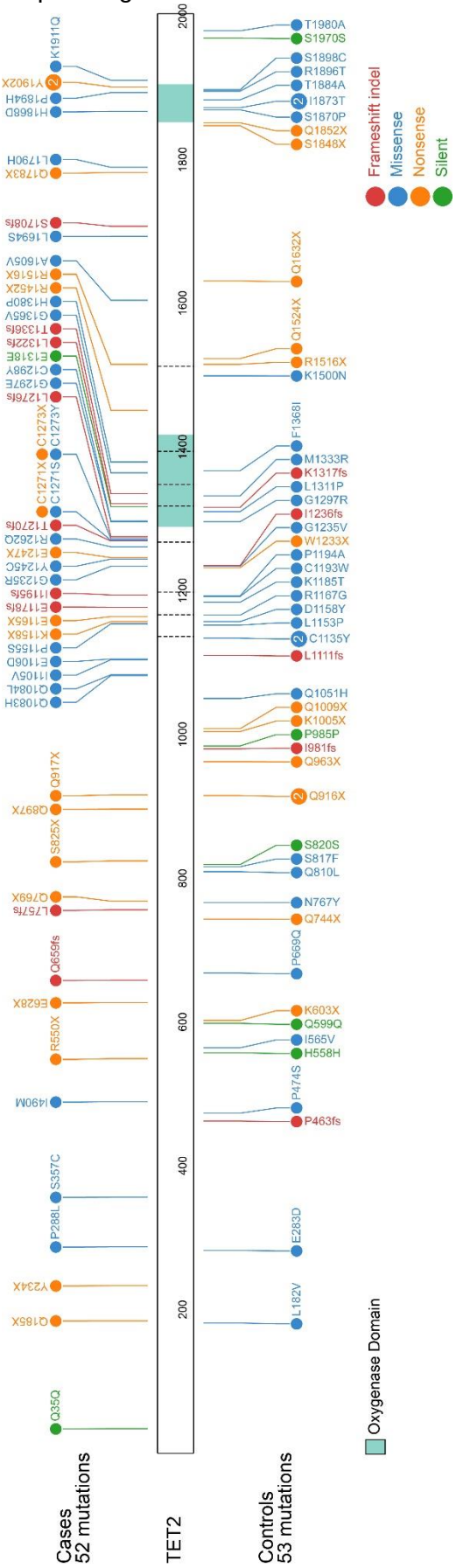
Supplementary Figure 3. The percentage of total alleles per case or control with exonic mutations in the respective genes, calculated across all matched case-control trios (including those with samples from both Nurses' Health Study collections) and color-coded by functional change.



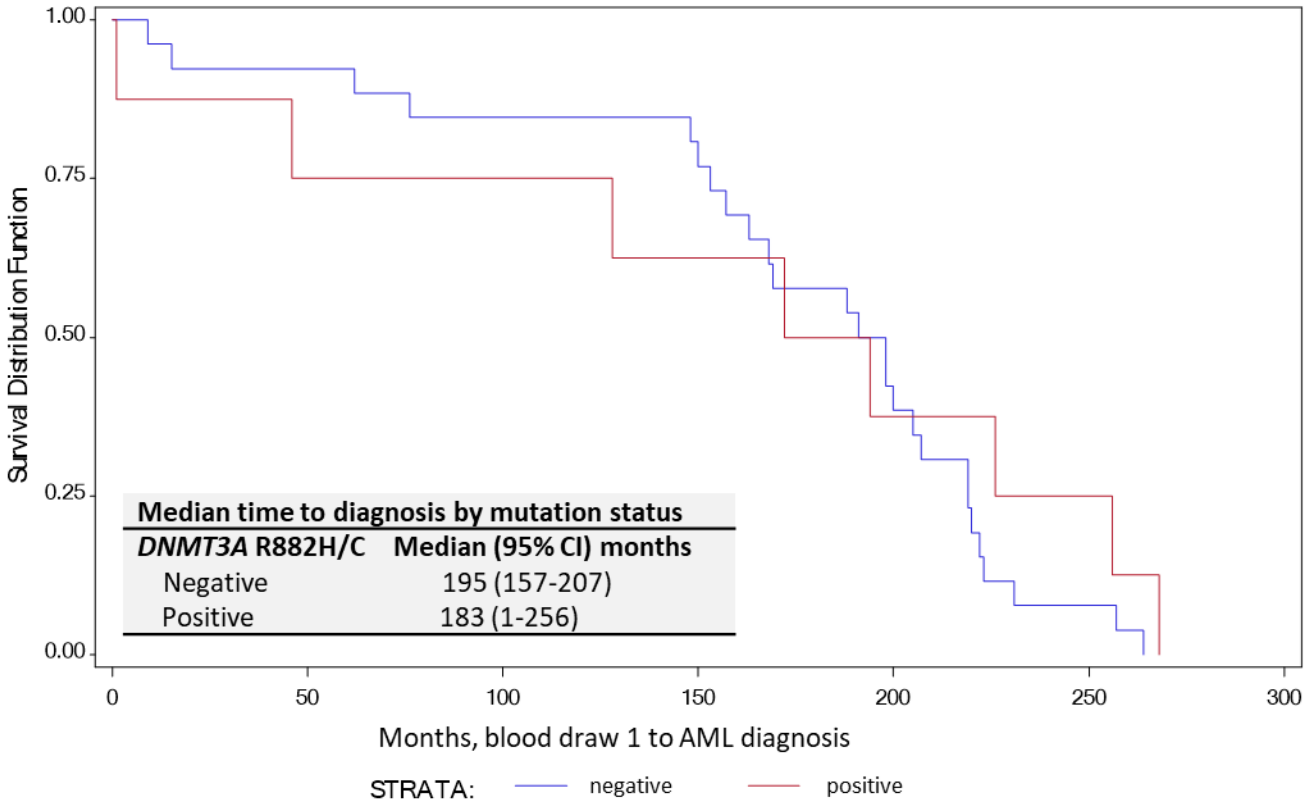
Supplementary Figure 4A. Lollipop plot depicting the amino acid sequence of *DNMT3A*, the most commonly mutated gene in this study sample, with the relative location of called exonic mutation plotted for cases (above the amino acid sequence) and controls (below the amino acid sequence).



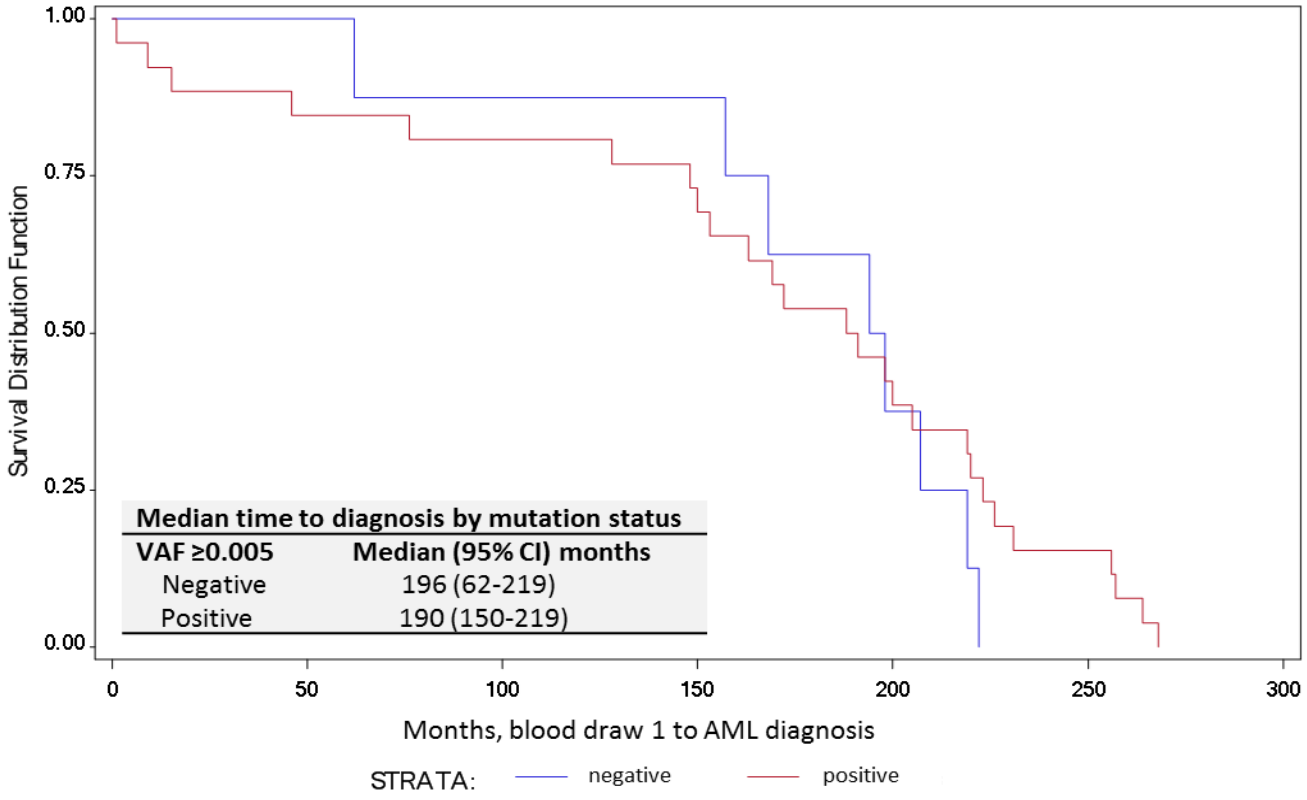
Supplementary Figure 4B. A lollipop plot depicting amino acid sequences from *TET2*, the second most commonly mutated gene in this study sample. Exonic mutations are scattered across the entire coding sequencing in both cases and controls.



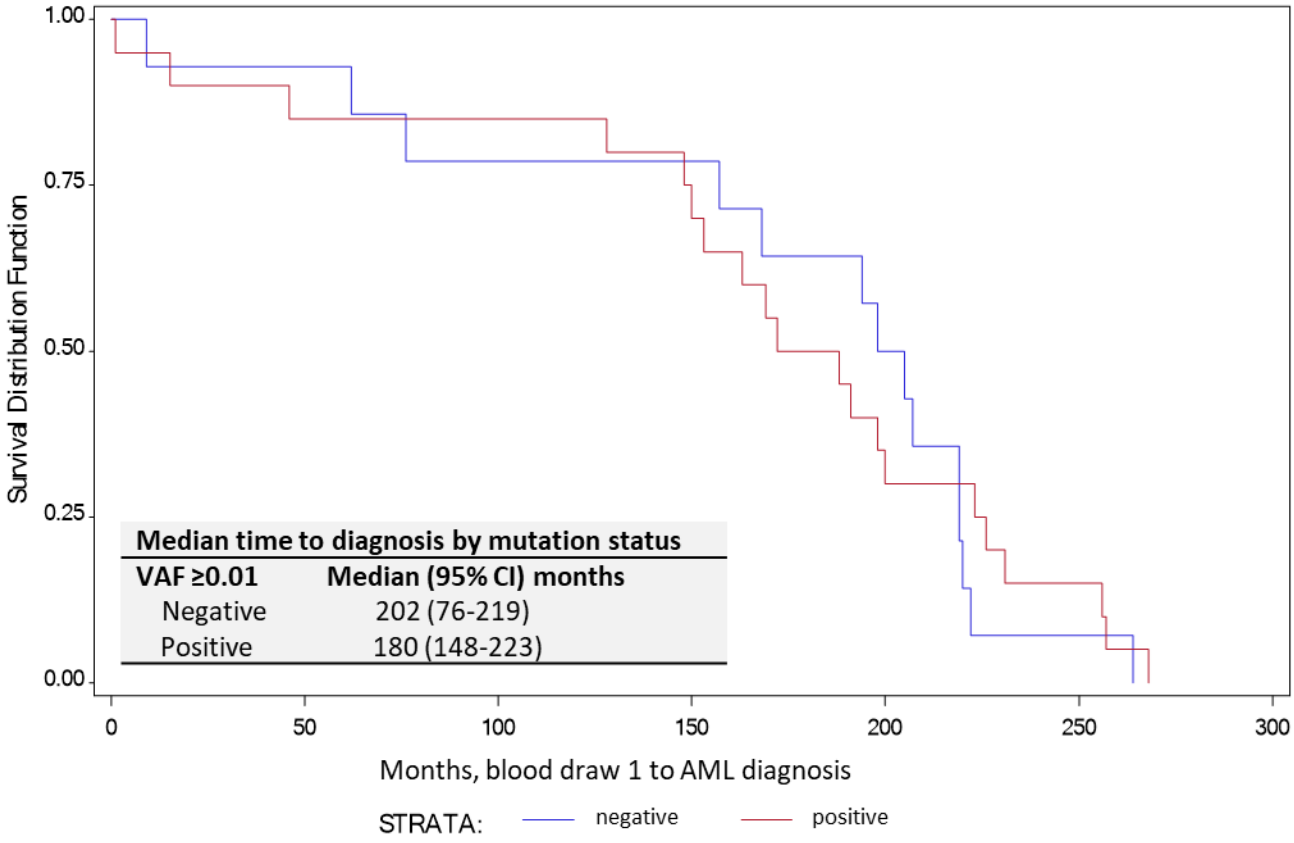
Supplementary Figure 5A. Time to acute myeloid leukemia (AML) diagnosis by pre-diagnosis *DNMT3A* R882H/C mutation status at one or both blood collections in Nurses' Health Study and Health Professionals Follow-up Study participants (AML cases only).



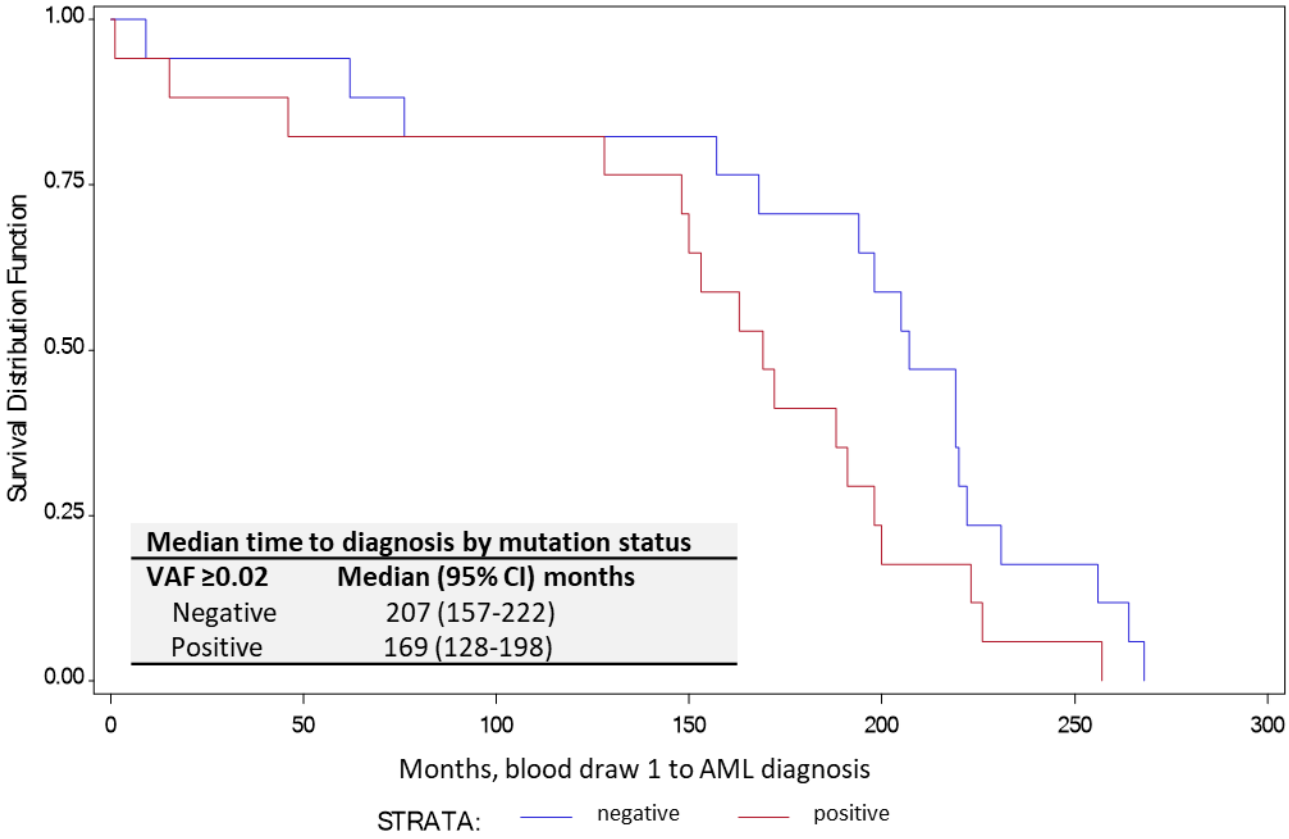
Supplementary Figure 5B. Time to acute myeloid leukemia (AML) diagnosis by pre-diagnosis detection of one or more mutations with an average variant allele fraction (VAF) of 0.005 or greater at one or both blood collections in Nurses' Health Study and Health Professionals Follow-up Study participants (AML cases only).



Supplementary Figure 5C. Time to AML diagnosis by pre-diagnosis detection of one or more mutations with an average variant allele fraction (VAF) of 0.01 or greater at one or both blood collections in Nurses' Health Study NHS and Health Professionals Follow-up Study participants (AML cases only).



Supplementary Figure 5D. Time to AML diagnosis by pre-diagnosis detection of one or more mutations with an average variant allele fraction (VAF) of 0.02 or greater at one or both blood collections in Nurses' Health Study NHS and Health Professionals Follow-up Study participants (AML cases only).



Supplementary Table 1. List of genomic regions captured by the Illumina TruSight Myeloid Sequencing Panel used for targeted error-corrected sequencing.

Gene	Target Region (exon)	Gene	Target Region (exon)
ABL1	4–6	*JAK3*	13
ASXL1	12	*KDM6A*	full
ATRX	8–10,17–31	*KIT*	2,8–11,13,17
BCOR	full	*KRAS*	2,3
BCORL1	full	*MLL*	5–8
BRAF	15	*MPL*	10
CALR	9	*MYD88*	3–5
CBL	8,9	*NOTCH1*	26-28,34
CBLB	9,10	*NPM1*	12
CBLC	9,10	*NRAS*	2,3
CDKN2A	full	*PDGFRA*	12,14,18
CEBPA	full	*PHF6*	full
CSF3R	14–17	*PTEN*	5,7
CUX1	full	*PTPN11*	3,13
DNMT3A	full	*RAD21*	full
ETV6/TEL	full	*RUNX1*	full
EZH2	full	*SETBP1*	4 (partial)
FBXW7	9–11	*SF3B1*	13–16
FLT3	14,15,20	*SMC1A*	2,11,16,17
GATA1	2	*SMC3*	10,13,19,23,25,28
GATA2	2–6	*SRSF2*	1
GNAS	8,9	*STAG2*	full
HRAS	2,3	*TET2*	3–11
IDH1	4	*TP53*	2–11
IDH2	4	*U2AF1*	2,6
IKZF1	full	*WT1*	7,9
JAK2	12,14	*ZRSR2*	full

Supplementary Table 2. Clonal mutations identified by error corrected sequencing in study participants. Each individual was identified by participant number, matched set number, and case/control status. Each mutation was identified by chromosome, position, nucleotide sequence change, associated gene, predicted annotation, and predicted amino acid sequence change (for exonic mutations). The average variant allele fraction (VAF) from two technical replicates was reported for mutations identified in the first collection or second collection.

Participant Number	Matched Set	Case/Control Status	Chromosome	Position	Reference	Alternate	Gene	Function	Amino Acid Change	COSMIC Annotation	Average VAF Collection 1	Average VAF Collection 2
1	3	Cntl 2	2	25463273	A	T	DNMT3A	exonic	D740E	NA	0.0010	
1	3	Cntl 2	2	25469492	C	A	DNMT3A	exonic	E426X	NA	0.0064	0.0486
1	3	Cntl 2	2	25470559	C	T	DNMT3A	exonic	W305X	COSM4383603	0.0145	0.0298
2	3	Cntl 1	11	119148891	T	C	CBL	exonic	Y371H	COSM34052		0.0026
2	3	Cntl 1	2	25462084	A	G	DNMT3A	exonic	S775P	NA	0.0101	0.0078
2	3	Cntl 1	2	25463283	A	C	DNMT3A	exonic	L737R	COSM87008	0.0036	0.0142
2	3	Cntl 1	4	106156519	C	T	TET2	exonic	P474S	NA	0.0003	
2	3	Cntl 1	X	15834073	A	C	ZRSR2	intronic	NA	NA		0.0003
2	3	Cntl 1	X	39932935	G	C	BCOR	exonic	T555S	NA		0.0003
2	3	Cntl 1	X	44733318	T	A	KDM6A	intronic	NA	NA	0.0097	0.0045
2	3	Cntl 1	X	129156967	G	A	BCORL1	intronic	NA	NA		0.0003
3	3	Case	17	7577124	C	T	TP53	exonic	V272M	COSM10891		0.0037
3	3	Case	2	25458613	C	A	DNMT3A	exonic	E854X	NA	0.0122	0.0257
3	3	Case	4	106164085	G	A	TET2	splicing	NA	NA	0.0021	
3	3	Case	4	106180783	T	A	TET2	exonic	C1271S	NA	0.0083	0.0042
3	3	Case	4	106180862	G	A	TET2	exonic	G1297E	NA		0.0013
3	3	Case	4	106182927	G	-	TET2	exonic	L1322fs	NA	0.0039	0.0126
4	4	Case	11	119148892	A	G	CBL	exonic	Y371C	COSM34054		0.0007
4	4	Case	2	25462023	C	T	DNMT3A	exonic	W795X	NA	0.0072	
4	4	Case	20	57484420	C	T	GNAS	exonic	R201C	COSM27887	0.0043	0.0035
4	4	Case	4	55561746	-	A	KIT	exonic	L46fs	NA		0.0022
4	4	Case	4	106157573	C	G	TET2	exonic	S825X	COSM87104	0.0007	
4	4	Case	4	106158348	G	T	TET2	exonic	Q1083H	NA		0.0015
4	4	Case	4	106158350	A	T	TET2	exonic	Q1084L	NA		0.0015
4	4	Case	4	106180782	-	TG	TET2	exonic	T1270fs	NA		0.0054
4	4	Case	4	106190861	A	C	TET2	exonic	H1380P	NA	0.0782	0.2199
4	4	Case	4	106193892	C	T	TET2	exonic	R1452X	COSM41706		0.0043
4	4	Case	X	133551310	A	T	PHF6	exonic	N316Y	NA		0.0028
5	4	Cntl 1	2	25457191	C	T	DNMT3A	exonic	R899H	COSM1583134	0.0034	0.0074
5	4	Cntl 1	2	25457249	T	C	DNMT3A	exonic	M880V	COSM120499	0.0015	
5	4	Cntl 1	2	25463239	A	G	DNMT3A	exonic	F752L	COSM133131	0.0015	0.0013
5	4	Cntl 1	2	25466800	G	A	DNMT3A	exonic	R635W	COSM87012		0.0015
5	4	Cntl 1	2	25467019	C	T	DNMT3A	intronic	NA	NA		0.0027
5	4	Cntl 1	2	25470582	C	T	DNMT3A	exonic	G298R	NA	0.0199	0.0100
5	4	Cntl 1	2	25470583	C	T	DNMT3A	exonic	W297X	NA	0.0197	0.0104
5	4	Cntl 1	X	129171440	G	A	BCORL1	exonic	W1468X	NA	0.0004	
6	4	Cntl 2	2	25467023	C	A	DNMT3A	splicing	NA	NA		0.0058

6	4	Cntl 2	7	101461023	G	T	CUX1	intronic	NA	NA		0.0012
7	5	Cntl 2	2	25464523	C	T	DNMT3A	exonic	E664K	COSM256045	0.0015	
7	5	Cntl 2	20	31023594	T	C	ASXL1	exonic	S1027P	NA	0.0007	
7	5	Cntl 2	3	128202803	C	T	GATA2	exonic	W306X	NA	0.0012	
7	5	Cntl 2	7	101877438	G	T	CUX1	exonic	E1180D	NA	0.0008	
7	5	Cntl 2	X	44921883	T	C	KDM6A	intronic	NA	NA	0.0010	
7	5	Cntl 2	X	44949247	C	A	KDM6A	intronic	NA	NA	0.0016	
8	5	Case	2	25463287	G	A	DNMT3A	exonic	R736C	COSM231560	0.0018	
8	5	Case	20	31022985	G	A	ASXL1	exonic	E824K	NA	0.0004	
8	5	Case	20	31024061	T	A	ASXL1	exonic	C1182X	NA	0.0009	
8	5	Case	4	106197348	C	A	TET2	exonic	P1894H	COSM87189	0.0013	
8	5	Case	7	50468102	A	T	IKZF1	exonic	Q446L	NA	0.0008	
8	5	Case	X	39931895	C	T	BCOR	exonic	E902K	NA	0.0014	
9	5	Cntl 1	10	89717854	A	G	PTEN	intronic	NA	NA	0.0008	
9	5	Cntl 1	2	25457176	G	A	DNMT3A	exonic	P904L	COSM87007	0.0046	
9	5	Cntl 1	2	25457177	G	A	DNMT3A	exonic	P904S	NA	0.0014	
9	5	Cntl 1	2	25457230	T	C	DNMT3A	exonic	Q886R	COSM4383519	0.0011	
9	5	Cntl 1	2	25463212	T	C	DNMT3A	exonic	M761V	NA	0.0019	
9	5	Cntl 1	3	38182392	T	C	MYD88	intronic	NA	NA	0.0004	
9	5	Cntl 1	4	106182913	C	A	TET2	intronic	NA	NA	0.0004	
9	5	Cntl 1	4	106197577	T	A	TET2	exonic	S1970S	NA	0.0011	
9	5	Cntl 1	7	101713725	G	A	CUX1	intronic	NA	NA	0.0008	
9	5	Cntl 1	9	139399412	C	A	NOTCH1	exonic	V1577V	NA	0.0011	
10	6	Cntl 2	17	7578280	G	T	TP53	exonic	P190H	COSM46283		0.0024
10	6	Cntl 2	2	25468904	A	-	DNMT3A	exonic	C487fs	NA		0.0046
10	6	Cntl 2	4	55593659	A	C	KIT	exonic	Q575H	NA	0.0010	
10	6	Cntl 2	4	106164069	T	G	TET2	exonic	C1193W	COSM42038		0.0006
10	6	Cntl 2	8	117878865	C	T	RAD21	exonic	C35Y	NA		0.0027
10	6	Cntl 2	X	44921878	T	C	KDM6A	intronic	NA	NA	0.0014	
10	6	Cntl 2	X	123181292	G	T	STAG2	exonic	R252R	NA		0.0023
11	6	Case	2	25462006	T	C	DNMT3A	exonic	M801V	NA	0.0016	0.0064
11	6	Case	2	25523115	G	T	DNMT3A	intronic	NA	NA		0.0014
11	6	Case	4	106155652	C	T	TET2	exonic	Q185X	NA		0.0048
11	6	Case	4	106158412	A	G	TET2	exonic	I1105V	NA		0.0007
11	6	Case	4	106162579	G	T	TET2	exonic	E1165X	NA		0.0123
11	6	Case	4	106164835	G	A	TET2	exonic	G1235R	COSM4383912		0.0006
11	6	Case	4	106196748	T	C	TET2	exonic	L1694S	COSM3824897		0.0010
11	6	Case	X	39932240	G	A	BCOR	exonic	P787S	NA		0.0039
11	6	Case	X	76888737	G	A	ATRX	exonic	R1698W	NA	0.0013	
11	6	Case	X	123191645	A	G	STAG2	intronic	NA	NA	0.0012	0.0076
12	6	Cntl 1	2	25458696	T	C	DNMT3A	splicing	NA	NA	0.0012	0.0018
12	6	Cntl 1	2	25462078	G	A	DNMT3A	exonic	P777S	NA		0.0023
12	6	Cntl 1	2	25466797	C	T	DNMT3A	exonic	V636M	COSM133124		0.0039
12	6	Cntl 1	2	25471019	G	A	DNMT3A	exonic	Q248X	NA		0.0011
12	6	Cntl 1	9	21994245	C	T	CDKN2A	exonic	R70Q	NA	0.0016	
13	7	Case	17	7578268	A	C	TP53	exonic	L194R	COSM44571		0.0135
13	7	Case	2	25462084	A	G	DNMT3A	exonic	S775P	NA		0.0011
13	7	Case	20	31023777	C	T	ASXL1	exonic	Q1088X	NA	0.0006	
13	7	Case	20	31023939	C	T	ASXL1	exonic	Q1142X	NA		0.0018

13	7	Case	4	106157076	G	-	TET2	exonic	Q659fs	NA	0.0065	0.0355
14	7	Cntl 2	11	118374162	C	A	KMT2A	exonic	R2516R	NA		0.0025
14	7	Cntl 2	2	25457192	G	A	DNMT3A	exonic	R899C	COSM5075581		0.0022
14	7	Cntl 2	2	25459874	C	A	DNMT3A	exonic	R803S	NA		0.0024
14	7	Cntl 2	2	25462006	T	C	DNMT3A	exonic	M801V	NA		0.0018
14	7	Cntl 2	2	25463308	G	C	DNMT3A	exonic	R729G	NA		0.0011
14	7	Cntl 2	2	25463508	C	T	DNMT3A	splicing	NA	NA		0.0013
14	7	Cntl 2	4	106164044	A	C	TET2	exonic	K1185T	COSM1618224		0.0006
15	7	Cntl 1	2	25463181	C	G	DNMT3A	exonic	R771P	NA		0.0005
15	7	Cntl 1	7	148506446	A	G	EZH2	exonic	I689T	NA		0.0015
15	7	Cntl 1	X	39932996	C	G	BCOR	exonic	A535P	NA		0.0005
16	8	Cntl 1	4	106182959	T	G	TET2	exonic	M1333R	NA	0.0178	0.0325
17	8	Case	2	25459810	C	T	DNMT3A	exonic	A825T	NA		0.0025
17	8	Case	2	25464568	C	A	DNMT3A	exonic	V649L	COSM4766071	0.0051	
17	8	Case	2	25467023	-	A	DNMT3A	splicing	NA	NA	0.0041	0.0101
17	8	Case	2	209113113	G	A	IDH1	exonic	R132C	COSM28747	0.0110	0.0239
17	8	Case	20	31024062	G	A	ASXL1	exonic	E1183K	NA	0.0016	
17	8	Case	4	106158417	G	T	TET2	exonic	E1106D	NA	0.0023	0.0104
17	8	Case	4	106180785	C	A	TET2	exonic	C1271X	NA		0.0009
17	8	Case	4	106196790	-	T	TET2	exonic	S1708fs	NA	0.0050	0.0084
17	8	Case	4	106197373	C	A	TET2	exonic	Y1902X	NA	0.0004	
17	8	Case	X	129147518	C	T	BCORL1	exonic	A257V	NA		0.0024
18	8	Cntl 2	2	25462068	A	G	DNMT3A	exonic	I780T	COSM1583121		0.0017
18	8	Cntl 2	4	55561767	G	A	KIT	exonic	E53K	NA		0.0006
18	8	Cntl 2	X	39932763	G	T	BCOR	exonic	T612T	NA		0.0012
18	8	Cntl 2	X	76874267	T	C	ATRX	intronic	NA	NA		0.0008
20	10	Cntl 2	2	25469541	C	T	DNMT3A	exonic	W409X	NA	0.0032	
20	10	Cntl 2	20	31023625	G	A	ASXL1	exonic	W1037X	COSM2270981	0.0010	
20	10	Cntl 2	7	101747667	T	A	CUX1	exonic	L153Q	NA	0.0056	
21	10	Cntl 1	2	25470554	G	C	DNMT3A	exonic	P307R	COSM221579	0.0009	
22	12	Cntl 1	2	25470584	C	T	DNMT3A	exonic	W297X	COSM133740	0.0094	
22	12	Cntl 1	4	106162492	A	G	TET2	UTR3	NA	NA	0.0011	
23	12	Case	10	112342324	C	T	SMC3	exonic	S243F	NA	0.0037	
23	12	Case	10	112360821	C	T	SMC3	exonic	L859L	NA	0.0025	
23	12	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.0034	
23	12	Case	2	25505567	T	-	DNMT3A	exonic	D64fs	NA	0.0037	
23	12	Case	20	31024062	G	A	ASXL1	exonic	E1183K	NA	0.0025	
23	12	Case	4	106155204	G	A	TET2	exonic	Q35Q	COSM3775459	0.0018	
23	12	Case	4	106162481	C	T	TET2	UTR3	NA	NA	0.0017	
23	12	Case	4	106180790	G	A	TET2	exonic	C1273Y	NA	0.0045	
23	12	Case	8	117875402	C	T	RAD21	exonic	A81T	NA	0.0030	
23	12	Case	X	39933592	G	A	BCOR	exonic	S336L	NA	0.0023	
23	12	Case	X	129148528	A	G	BCORL1	exonic	T594A	NA	0.0131	
24	12	Cntl 2	20	31024062	G	A	ASXL1	exonic	E1183K	NA	0.0014	
24	12	Cntl 2	3	105439182	A	G	CBLB	intronic	NA	NA	0.3513	
24	12	Cntl 2	4	106157845	C	T	TET2	exonic	Q916X	COSM43417	0.0058	
25	13	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944		0.0025
25	13	Case	2	25463286	C	T	DNMT3A	exonic	R736H	COSM133737		0.0034
25	13	Case	2	25466797	C	G	DNMT3A	exonic	V636L	NA	0.0020	

25	13	Case	2	25466824	GGACAGGTGGGTAAACCTTT	-	DNMT3A	exonic	P620fs	NA		0.0045
25	13	Case	20	31024062	G	A	ASXL1	exonic	E1183K	NA	0.0012	
25	13	Case	3	38182641	T	C	MYD88	exonic	X205R	COSM85940	0.0043	0.0033
25	13	Case	4	106164053	A	T	TET2	exonic	K1158X	NA	0.0011	
25	13	Case	4	106164086	T	C	TET2	splicing	NA	NA		0.0038
25	13	Case	4	106180791	T	A	TET2	exonic	C1273X	NA		0.0016
25	13	Case	X	39933021	C	T	BCOR	exonic	S526S	COSM5367089	0.0019	0.0037
26	13	Cntl 1	13	28608282	C	T	FLT3	exonic	V592I	COSM4166487		0.0053
26	13	Cntl 1	2	25458595	A	G	DNMT3A	exonic	W860R	COSM231568	0.0014	
26	13	Cntl 1	4	106157398	A	T	TET2	exonic	N767Y	NA	0.0005	
26	13	Cntl 1	7	50444334	G	C	IKZF1	exonic	S88S	NA		0.0004
26	13	Cntl 1	7	101833193	C	T	CUX1	intronic	NA	NA	0.0018	
26	13	Cntl 1	X	44870368	A	G	KDM6A	intronic	NA	NA		0.0024
26	13	Cntl 1	X	129171492	G	A	BCORL1	exonic	A1486T	NA	0.0021	0.0010
27	13	Cntl 2	20	31023702	C	T	ASXL1	exonic	Q1063X	COSM159235		0.0008
27	13	Cntl 2	21	36164855	G	A	RUNX1	exonic	P340P	NA	0.0004	
27	13	Cntl 2	4	106164836	G	T	TET2	exonic	G1235V	NA	0.0011	
27	13	Cntl 2	X	129184866	C	T	BCORL1	intronic	NA	NA		0.0019
28	15	Cntl 2	17	7577037	G	T	TP53	exonic	P301T	COSM46137		0.0021
28	15	Cntl 2	2	25469646	C	G	DNMT3A	splicing	NA	NA	0.0024	0.0075
28	15	Cntl 2	2	25505603	C	T	DNMT3A	intronic	NA	NA		0.0026
28	15	Cntl 2	2	25505625	G	A	DNMT3A	intronic	NA	NA		0.0029
28	15	Cntl 2	3	128205273	A	G	GATA2	intronic	NA	NA		0.0008
29	15	Cntl 1	11	119149239	G	C	CBL	exonic	C416S	NA	0.0048	0.0077
29	15	Cntl 1	17	7577228	A	G	TP53	intronic	NA	NA	0.0007	
29	15	Cntl 1	2	25462020	C	T	DNMT3A	exonic	G796D	NA		0.0026
29	15	Cntl 1	2	25466797	C	A	DNMT3A	exonic	V636L	NA	0.0012	0.0029
30	15	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.0036	0.0165
30	15	Case	2	25464538	G	C	DNMT3A	exonic	R659G	NA		0.0045
30	15	Case	2	25467448	C	A	DNMT3A	exonic	G543V	COSM249135		0.0032
31	16	Case	10	112342324	C	T	SMC3	exonic	S243F	NA	0.0031	
31	16	Case	2	25468935	T	C	DNMT3A	splicing	NA	NA		0.0016
31	16	Case	2	25470559	C	T	DNMT3A	exonic	W305X	COSM4383603		0.0016
31	16	Case	20	31024062	G	A	ASXL1	exonic	E1183K	NA	0.0013	
31	16	Case	7	148512028	C	G	EZH2	exonic	K550N	NA	0.0020	
31	16	Case	X	44733279	G	T	KDM6A	intronic	NA	NA	0.0017	
31	16	Case	X	44937714	A	-	KDM6A	exonic	T968fs	NA	0.0075	
31	16	Case	X	123197118	G	A	STAG2	intronic	NA	NA	0.0051	0.0063
32	16	Cntl 2	2	25457162	A	G	DNMT3A	exonic	F909L	NA	0.0731	0.2689
32	16	Cntl 2	2	25463541	G	C	DNMT3A	exonic	S714C	COSM87011	0.0076	0.0065
32	16	Cntl 2	2	25470039	A	T	DNMT3A	intronic	NA	NA	0.0046	
32	16	Cntl 2	3	128202820	G	A	GATA2	exonic	A300A	NA		0.0008
32	16	Cntl 2	4	106158503	G	A	TET2	exonic	C1135Y	COSM166289		0.0030
32	16	Cntl 2	X	15833889	G	A	ZRSR2	exonic	R216K	NA		0.0004
33	16	Cntl 1	17	7576645	A	G	TP53	exonic	F336L	NA		0.0019
33	16	Cntl 1	2	25467023	C	-	DNMT3A	splicing	NA	NA		0.0032

33	16	Cntl 1	2	25470029	T	C	DNMT3A	splicing	NA	NA		0.0029
33	16	Cntl 1	2	25505563	C	A	DNMT3A	exonic	T65T	COSM4769280	0.0016	
33	16	Cntl 1	4	106157105	C	A	TET2	exonic	P669Q	NA	0.0008	
33	16	Cntl 1	4	106157559	T	C	TET2	exonic	S820S	NA		0.0005
33	16	Cntl 1	4	106158040	ATTAAGGTGGAACCTGG	-	TET2	exonic	I981fs	NA	0.0024	0.0023
33	16	Cntl 1	4	106158571	G	T	TET2	exonic	D1158Y	COSM4430996	0.0021	
33	16	Cntl 1	4	106197210	C	A	TET2	exonic	S1848X	NA	0.0024	
33	16	Cntl 1	4	106197221	C	T	TET2	exonic	Q1852X	COSM42076	0.0012	
33	16	Cntl 1	7	101917607	G	T	CUX1	intronic	NA	NA	0.0013	
33	16	Cntl 1	7	148512121	A	T	EZH2	exonic	S519S	NA	0.0011	
35	17	Cntl 1	2	25458661	T	C	DNMT3A	exonic	N838D	COSM231575	0.0030	0.0035
35	17	Cntl 1	4	106197317	A	G	TET2	exonic	T1884A	COSM42070		0.0013
36	17	Case	2	25462018	T	C	DNMT3A	exonic	N797D	NA	0.0061	0.0025
36	17	Case	2	25463182	G	A	DNMT3A	exonic	R771X	COSM231563	0.0089	0.0071
36	17	Case	2	25470559	C	T	DNMT3A	exonic	W305X	COSM4383603	0.0044	
36	17	Case	4	106155801	T	A	TET2	exonic	Y234X	NA	0.0024	
36	17	Case	7	50358764	A	G	IKZF1	intronic	NA	NA	0.0006	
36	17	Case	7	148511184	G	A	EZH2	exonic	T573I	COSM133043	0.0020	
36	17	Case	8	117869784	T	C	RAD21	intronic	NA	NA	0.0032	0.0036
36	17	Case	X	123234525	G	C	STAG2	UTR3	NA	NA	0.0004	
37	20	Cntl 1	1	36933189	C	T	CSF3R	exonic	C643Y	NA	0.0046	0.0059
37	20	Cntl 1	12	25398284	C	T	KRAS	exonic	G12D	COSM521	0.0039	0.0071
37	20	Cntl 1	12	112888207	G	C	PTPN11	exonic	A75P	NA		0.0004
37	20	Cntl 1	2	25463298	A	C	DNMT3A	exonic	F732C	NA	0.0006	0.0015
37	20	Cntl 1	2	25464494	G	A	DNMT3A	exonic	G673G	NA	0.0019	0.0041
37	20	Cntl 1	2	25464495	C	A	DNMT3A	exonic	G673V	NA	0.0019	0.0040
37	20	Cntl 1	4	106158503	G	A	TET2	exonic	C1135Y	COSM166289		0.0035
37	20	Cntl 1	X	39933206	C	T	BCOR	exonic	V465I	NA		0.0020
37	20	Cntl 1	X	123197128	A	T	STAG2	intronic	NA	NA		0.0021
37	20	Cntl 1	X	129162713	T	C	BCORL1	exonic	D1394D	COSM4106597	0.0010	0.0026
37	20	Cntl 1	X	129185929	G	C	BCORL1	exonic	M1597I	NA		0.0012
38	20	Cntl 2	2	25470480	C	T	DNMT3A	exonic	G332R	COSM2270955	0.0187	0.0181
39	20	Case	12	112888371	C	A	PTPN11	intronic	NA	NA	0.0014	
39	20	Case	13	28608152	G	A	FLT3	intronic	NA	NA		0.0031
39	20	Case	15	90631934	C	T	IDH2	exonic	R140Q	COSM41590		0.0262
39	20	Case	17	74732959	G	T	SRSF2	exonic	P95H	COSM211504		0.2521
39	20	Case	2	25462050	G	C	DNMT3A	exonic	S786X	NA	0.0009	0.0008
39	20	Case	2	25462077	G	C	DNMT3A	exonic	P777R	NA	0.0026	0.0063
39	20	Case	2	25463184	G	A	DNMT3A	exonic	S770L	COSM231549	0.0014	
39	20	Case	20	31022757	C	T	ASXL1	exonic	Q748X	COSM307766	0.0009	
39	20	Case	21	36421254	A	G	RUNX1	UTR5	NA	NA	0.0003	
39	20	Case	4	106196213	C	T	TET2	exonic	R1516X	COSM43420	0.0032	0.0052
39	20	Case	4	106197014	C	T	TET2	exonic	Q1783X	NA		0.0015
39	20	Case	7	101801902	C	T	CUX1	intronic	NA	NA	0.0016	
39	20	Case	7	148523660	C	T	EZH2	exonic	D265N	NA	0.0012	
39	20	Case	X	44929259	A	T	KDM6A	exonic	K787X	NA	0.0012	
40	21	Cntl 2	11	119149235	G	C	CBL	exonic	G415R	NA	0.0012	

40	21	Cntl 2	17	7577114	C	T	TP53	exonic	C275Y	COSM10893		0.0016
40	21	Cntl 2	2	25463248	G	A	DNMT3A	exonic	R749C	COSM219133	0.0019	0.0014
40	21	Cntl 2	2	25467492	G	T	DNMT3A	exonic	Y528X	NA		0.0008
40	21	Cntl 2	2	25470498	G	A	DNMT3A	exonic	R326C	COSM4169721		0.0028
40	21	Cntl 2	3	128202818	G	A	GATA2	exonic	T301I	NA	0.0011	
40	21	Cntl 2	4	106156792	A	G	TET2	exonic	I565V	NA	0.0009	
40	21	Cntl 2	4	106158112	A	T	TET2	exonic	K1005X	NA	0.0046	0.0087
40	21	Cntl 2	4	106196161	A	G	TET2	intronic	NA	NA	0.0004	
40	21	Cntl 2	7	101821838	G	C	CUX1	exonic	V306V	NA	0.0012	
40	21	Cntl 2	X	129149049	C	G	BCORL1	exonic	G767G	NA	0.0008	
41	21	Cntl 1	17	7578280	G	C	TP53	exonic	P190R	COSM44004		0.0014
41	21	Cntl 1	4	106164840	CC	-	TET2	exonic	I1236fs	NA	0.0209	0.0257
41	21	Cntl 1	7	50468197	A	G	IKZF1	exonic	T478A	NA		0.0007
42	21	Case	17	74732959	G	A	SRSF2	exonic	P95L	COSM146288		0.2992
42	21	Case	4	106180798	C	-	TET2	exonic	L1276fs	NA	0.0057	
42	21	Case	4	106182969	-	T	TET2	exonic	T1336fs	NA	0.0035	
42	21	Case	7	148512107	T	A	EZH2	exonic	N524I	NA	0.0003	
42	21	Case	X	39921444	T	C	BCOR	exonic	N1425S	COSM403987		0.0608
43	22	Case	10	112342324	C	T	SMC3	exonic	S243F	NA	0.0042	
43	22	Case	2	25468135	C	T	DNMT3A	exonic	C514Y	NA	0.0066	
43	22	Case	4	106156569	A	G	TET2	exonic	I490M	NA	0.0004	
43	22	Case	X	76813233	T	C	ATRX	intronic	NA	NA	0.0020	
44	22	Cntl 2	4	106180861	G	A	TET2	exonic	G1297R	NA	0.0064	
45	22	Cntl 1	4	106164831	G	A	TET2	exonic	W1233X	COSM211667	0.0007	
45	22	Cntl 1	7	101840575	C	A	CUX1	exonic	G628G	NA	0.0014	
45	22	Cntl 1	X	44733237	A	T	KDM6A	intronic	NA	NA	0.0024	
45	22	Cntl 1	X	44929404	A	C	KDM6A	exonic	Q835P	NA	0.0003	
46	11	Cntl 1	17	7578406	C	T	TP53	exonic	R175H	COSM10648		0.0034
46	11	Cntl 1	19	13054624	A	G	CALR	exonic	D384G	NA		0.0015
46	11	Cntl 1	2	25458595	A	G	DNMT3A	exonic	W860R	COSM231568		0.0024
46	11	Cntl 1	2	25468159	T	C	DNMT3A	exonic	H506R	NA		0.0232
46	11	Cntl 1	2	25468186	C	T	DNMT3A	exonic	C497Y	COSM1318925		0.0034
46	11	Cntl 1	4	106158509	G	A	TET2	splicing	NA	COSM87117		0.0233
46	11	Cntl 1	4	106164070	C	G	TET2	exonic	P1194A	NA		0.0008
47	11	Cntl 2	2	25467198	G	C	DNMT3A	exonic	C559W	NA		0.0007
47	11	Cntl 2	2	25468166	G	-	DNMT3A	exonic	L504fs	NA		0.0177
47	11	Cntl 2	4	106197285	T	C	TET2	exonic	I1873T	COSM41741		0.0071
47	11	Cntl 2	X	44732893	C	T	KDM6A	exonic	G32G	NA		0.0023
48	11	Case	21	36171607	G	A	RUNX1	exonic	R320X	COSM41699		0.0020
48	11	Case	21	36171718	G	A	RUNX1	exonic	Q283X	NA		0.0026
48	11	Case	21	36231774	G	A	RUNX1	exonic	R204X	COSM25124		0.0280
48	11	Case	21	36231859	-	A	RUNX1	exonic	L175fs	NA		0.1721
48	11	Case	21	36259172	G	A	RUNX1	exonic	R107C	COSM24736		0.0093
48	11	Case	21	36259175	A	G	RUNX1	exonic	W106R	COSM1180473		0.0027
48	11	Case	21	36259200	GAAGT T	-	RUNX1	exonic	96_97del	NA		0.0120
48	11	Case	X	123215360	C	A	STAG2	exonic	A969D	NA		0.0144
48	11	Case	X	123227870	G	A	STAG2	exonic	R1157Q	NA		0.0021
48	11	Case	X	129147263	A	G	BCORL1	exonic	N172S	NA		0.0010
49	104	Cntl 2										

50	104	Case	17	7577556	C	G	TP53	exonic	C242S	COSM11133	0.0008
50	104	Case	4	106180931	G	A	TET2	intronic	NA	NA	0.0017
50	104	Case	4	106196481	C	T	TET2	exonic	A1605V	NA	0.0030
50	104	Case	4	106197269	C	G	TET2	exonic	H1868D	NA	0.0046
50	104	Case	7	148512130	G	A	EZH2	exonic	D516D	NA	0.0016
50	104	Case	8	117859819	G	A	RAD21	exonic	Q606X	NA	0.0007
50	104	Case	9	5073770	G	T	JAK2	exonic	V617F	COSM12600	0.0809
50	104	Case	X	15840967	G	C	ZRSR2	exonic	D351H	NA	0.0007
51	104	Cntl 1	2	25457243	G	A	DNMT3A	exonic	R882C	COSM53042	0.0701
51	104	Cntl 1	2	25466788	G	A	DNMT3A	exonic	L639F	NA	0.0024
51	104	Cntl 1	X	39916541	A	T	BCOR	exonic	C1454S	NA	0.0033
52	110	Case	2	25457243	G	A	DNMT3A	exonic	R882C	COSM53042	0.0031
52	110	Case	2	25458696	T	G	DNMT3A	splicing	NA	NA	0.0005
52	110	Case	2	25463286	C	T	DNMT3A	exonic	R736H	COSM133737	0.0028
52	110	Case	2	25463532	T	C	DNMT3A	exonic	N717S	COSM1583099	0.0011
52	110	Case	2	25469614	G	-	DNMT3A	exonic	P385fs	COSM1717669	0.0082
52	110	Case	21	44514777	T	G	U2AF1	exonic	Q157P	COSM211534	0.0044
52	110	Case	9	5073770	G	T	JAK2	exonic	V617F	COSM12600	0.0278
52	110	Case	X	15838377	A	G	ZRSR2	exonic	Y292C	NA	0.0177
52	110	Case	X	129146951	G	A	BCORL1	exonic	G68D	NA	0.0030
53	110	Cntl 1									
54	110	Cntl 2	11	119148930	T	G	CBL	exonic	C384G	NA	0.0008
54	110	Cntl 2	2	25466799	C	G	DNMT3A	exonic	R635P	COSM231550	0.0011
54	110	Cntl 2	7	101845544	G	A	CUX1	intronic	NA	NA	0.0008
54	110	Cntl 2	X	129148435	A	G	BCORL1	exonic	T563A	NA	0.0012
55	103	Cntl 1	2	25461994	C	G	DNMT3A	intronic	NA	NA	0.0006
55	103	Cntl 1	4	106197360	C	G	TET2	exonic	S1898C	NA	0.0002
55	103	Cntl 1	7	101822027	A	G	CUX1	intronic	NA	NA	0.0005
55	103	Cntl 1	X	129148468	A	G	BCORL1	exonic	S574G	NA	0.0005
56	103	Case	2	25457176	G	A	DNMT3A	exonic	P904L	COSM87007	0.0153
56	103	Case	2	25461998	C	G	DNMT3A	splicing	NA	NA	0.0008
56	103	Case	4	106156168	A	T	TET2	exonic	S357C	NA	0.0004
56	103	Case	9	5073770	G	T	JAK2	exonic	V617F	COSM12600	0.0245
57	103	Cntl 2	11	119148911	A	T	CBL	exonic	T377T	NA	0.0014
57	103	Cntl 2	12	112888215	G	T	PTPN11	exonic	L77F	NA	0.0015
57	103	Cntl 2	19	33792351	G	T	CEBPA	exonic	L324M	NA	0.0007
57	103	Cntl 2	2	25463242	A	C	DNMT3A	exonic	F751V	COSM4766069	0.0010
57	103	Cntl 2	21	36259235	G	T	RUNX1	exonic	P86T	NA	0.0011
57	103	Cntl 2	4	106180923	AG	-	TET2	exonic	K1317fs	NA	0.0025
57	103	Cntl 2	4	106190824	T	A	TET2	exonic	F1368I	NA	0.0065
57	103	Cntl 2	X	39923696	A	T	BCOR	exonic	V1132E	NA	0.0022
58	117	Case	17	7578485	A	G	TP53	exonic	S149P	COSM45352	0.0006
58	117	Case	20	31023757	T	C	ASXL1	exonic	L1081P	NA	0.0003
58	117	Case	21	36231812	C	G	RUNX1	exonic	R191T	NA	0.0014
58	117	Case	3	38181994	G	A	MYD88	exonic	V206V	NA	0.0007
58	117	Case	4	106155962	C	T	TET2	exonic	P288L	NA	0.0023
58	117	Case	X	39932342	C	G	BCOR	exonic	A753P	NA	0.0010
58	117	Case	X	129149047	G	A	BCORL1	exonic	G767S	NA	0.0023
59	117	Cntl 1	11	119149062	G	A	CBL	intronic	NA	NA	0.0023

59	117	Cntl 1	2	25458595	A	G	DNMT3A	exonic	W860R	COSM231568	0.0087
59	117	Cntl 1	2	25463286	C	T	DNMT3A	exonic	R736H	COSM133737	0.0019
59	117	Cntl 1	2	25464435	-	TC	DNMT3A	exonic	K693fs	NA	0.0052
59	117	Cntl 1	2	25464544	C	T	DNMT3A	exonic	V657M	NA	0.0045
59	117	Cntl 1	4	106157549	C	T	TET2	exonic	S817F	NA	0.0009
59	117	Cntl 1	7	148512621	C	A	EZH2	exonic	C508F	NA	0.0007
60	117	Cntl 2	2	25458627	G	C	DNMT3A	exonic	P849R	COSM133130	0.0013
60	117	Cntl 2	4	106196213	C	T	TET2	exonic	R1516X	COSM43420	0.0023
61	105	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.2909
61	105	Case	4	106156747	C	T	TET2	exonic	R550X	COSM41644	0.0023
61	105	Case	4	106164917	G	A	TET2	exonic	R1262Q	NA	0.0013
61	105	Case	8	117870530	T	C	RAD21	intronic	NA	NA	0.0709
62	105	Cntl 1	2	25463287	G	A	DNMT3A	exonic	R736C	COSM231560	0.0042
63	105	Cntl 2	7	50367337	G	A	IKZF1	exonic	K48K	NA	0.0004
63	105	Cntl 2	9	139397000	C	A	NOTCH1	intronic	NA	NA	0.0014
64	118	Case	1	115258763	C	T	NRAS	exonic	V7M	NA	0.0007
64	118	Case	17	74732959	G	C	SRSF2	exonic	P95R	COSM211661	0.0024
64	118	Case	2	25469631	G	C	DNMT3A	exonic	R379R	NA	0.0008
64	118	Case	2	198266606	C	G	SF3B1	exonic	A744P	COSM4383628	0.0038
64	118	Case	7	101924205	T	C	CUX1	intronic	NA	NA	0.0006
64	118	Case	X	123159834	T	C	STAG2	intronic	NA	NA	0.0020
65	118	Cntl 1	10	112344070	T	C	SMC3	exonic	N407N	NA	0.0006
65	118	Cntl 1	2	25458595	A	G	DNMT3A	exonic	W860R	COSM231568	0.0013
65	118	Cntl 1	2	25463223	T	-	DNMT3A	exonic	N757fs	NA	0.0049
65	118	Cntl 1	2	25463508	C	T	DNMT3A	splicing	NA	NA	0.0051
65	118	Cntl 1	7	148506296	G	A	EZH2	intronic	NA	NA	0.0087
65	118	Cntl 1	9	139399213	G	A	NOTCH1	exonic	L1644L	NA	0.0013
65	118	Cntl 1	9	139399217	G	C	NOTCH1	exonic	D1642E	NA	0.0008
66	118	Cntl 2	17	7577539	G	A	TP53	exonic	R248W	COSM10656	0.0008
66	118	Cntl 2	2	25462068	A	G	DNMT3A	exonic	I780T	COSM1583121	0.0218
66	118	Cntl 2	4	106156486	C	-	TET2	exonic	P463fs	NA	0.0273
66	118	Cntl 2	4	106197275	T	C	TET2	exonic	S1870P	COSM211749	0.0015
67	116	Cntl 1	17	7577120	C	T	TP53	exonic	R273H	COSM10660	0.0063
67	116	Cntl 1	2	25463227	C	G	DNMT3A	exonic	E756Q	NA	0.0030
67	116	Cntl 1	2	25470590	A	G	DNMT3A	exonic	L295P	NA	0.0086
67	116	Cntl 1	2	25523076	C	A	DNMT3A	exonic	E37X	NA	0.0025
67	116	Cntl 1	20	57484421	G	A	GNAS	exonic	R201H	COSM27895	0.0037
67	116	Cntl 1	7	148506191	T	C	EZH2	exonic	T723A	NA	0.0005
67	116	Cntl 1	X	44732901	A	G	KDM6A	exonic	E35G	NA	0.0019
67	116	Cntl 1	X	76849179	T	C	ATRX	exonic	I2033V	NA	0.0009
68	116	Case	2	25462080	T	C	DNMT3A	exonic	N776S	NA	0.0005
68	116	Case	2	25463296	C	A	DNMT3A	exonic	E733X	NA	0.0022
68	116	Case	21	44524456	G	A	U2AF1	exonic	S34F	COSM166866	0.0098
68	116	Case	7	148515266	A	T	EZH2	intronic	NA	NA	0.0007
68	116	Case	X	76855131	A	T	ATRX	intronic	NA	NA	0.0007
68	116	Case	X	123190086	G	A	STAG2	splicing	NA	NA	0.0009
68	116	Case	X	129155067	G	T	BCORL1	exonic	R1183R	NA	0.0011
69	116	Cntl 2	10	112361903	G	C	SMC3	exonic	R1024R	NA	0.0053
69	116	Cntl 2	2	25463287	G	A	DNMT3A	exonic	R736C	COSM231560	0.0004

69	116	Cntl 2	2	25466797	C	T	DNMT3A	exonic	V636M	COSM133124	0.0031
69	116	Cntl 2	4	106180904	T	C	TET2	exonic	L1311P	NA	0.0011
69	116	Cntl 2	4	153249571	G	T	FBXW7	intronic	NA	NA	0.0030
69	116	Cntl 2	7	101740748	T	A	CUX1	exonic	Y125N	NA	0.0028
69	116	Cntl 2	7	101844758	C	T	CUX1	exonic	A727A	NA	0.0007
69	116	Cntl 2	7	101844907	C	G	CUX1	exonic	A777G	NA	0.0004
70	109	Cntl 1	X	123171513	G	A	STAG2	intronic	NA	NA	0.0013
71	109	Cntl 2	12	12022838	T	C	ETV6	exonic	M315T	NA	0.0009
71	109	Cntl 2	17	7577114	C	T	TP53	exonic	C275Y	COSM10893	0.0055
71	109	Cntl 2	17	7578518	C	T	TP53	exonic	A138T	COSM44821	0.0078
71	109	Cntl 2	17	7578519	C	G	TP53	exonic	L137L	NA	0.0078
71	109	Cntl 2	2	25458595	A	G	DNMT3A	exonic	W860R	COSM231568	0.0010
71	109	Cntl 2	2	198267469	T	C	SF3B1	exonic	R630G	NA	0.0044
71	109	Cntl 2	21	44524456	G	A	U2AF1	exonic	S34F	COSM166866	0.0008
71	109	Cntl 2	4	106156896	A	G	TET2	exonic	Q599Q	NA	0.0002
71	109	Cntl 2	4	106158432	A	-	TET2	exonic	L1111fs	NA	0.0103
71	109	Cntl 2	7	101877438	G	A	CUX1	exonic	E1180E	NA	0.0005
72	109	Case	1	36932494	G	C	CSF3R	exonic	Q686E	NA	0.0015
72	109	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.0027
72	109	Case	2	25458586	C	T	DNMT3A	exonic	E863K	COSM1583127	0.0017
72	109	Case	2	25459875	C	A	DNMT3A	splicing	NA	NA	0.0024
72	109	Case	2	25462068	A	G	DNMT3A	exonic	I780T	COSM1583121	0.0021
72	109	Case	2	25462075	C	A	DNMT3A	exonic	V778L	NA	0.0004
72	109	Case	2	25463308	G	A	DNMT3A	exonic	R729W	COSM249142	0.0019
72	109	Case	2	25469647	T	C	DNMT3A	splicing	NA	COSM133125	0.0392
72	109	Case	2	25470498	G	A	DNMT3A	exonic	R326C	COSM4169721	0.0022
72	109	Case	2	198266611	C	T	SF3B1	exonic	G742D	COSM145923	0.0026
72	109	Case	X	44918688	G	A	KDM6A	exonic	A391T	NA	0.0036
73	114	Case	X	53423471	G	A	SMC1A	exonic	H877Y	NA	0.0099
74	114	Cntl 1	4	106155948	G	T	TET2	exonic	E283D	NA	0.0007
74	114	Cntl 1	X	44732886	C	T	KDM6A	exonic	A30V	COSM3364006	0.0036
75	114	Cntl 2	2	25462068	A	G	DNMT3A	exonic	I780T	COSM1583121	0.0009
75	114	Cntl 2	2	25463225	C	G	DNMT3A	exonic	E756D	NA	0.0005
75	114	Cntl 2	2	25463296	-	A	DNMT3A	exonic	E733_F734delinsX	COSM53095	0.0037
75	114	Cntl 2	2	25467448	C	G	DNMT3A	exonic	G543A	COSM256033	0.0009
75	114	Cntl 2	4	106157329	C	T	TET2	exonic	Q744X	COSM4169860	0.0016
76	112	Cntl 1	2	25470028	C	G	DNMT3A	splicing	NA	NA	0.0067
76	112	Cntl 1	4	106158124	C	T	TET2	exonic	Q1009X	NA	0.0007
76	112	Cntl 1	4	106197605	A	G	TET2	exonic	T1980A	NA	0.0022
76	112	Cntl 1	9	139391190	G	A	NOTCH1	exonic	P2334L	NA	0.0009
76	112	Cntl 1	X	15818051	G	A	ZRSR2	exonic	E60K	NA	0.0056
77	112	Case	15	90631934	C	T	IDH2	exonic	R140Q	COSM41590	0.0034
77	112	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.3281
77	112	Case	2	198266611	C	T	SF3B1	exonic	G742D	COSM145923	0.0047
77	112	Case	2	198266834	T	C	SF3B1	exonic	K700E	COSM84677	0.0043
77	112	Case	21	44514777	T	C	U2AF1	exonic	Q157R	COSM211532	0.0209
77	112	Case	3	38182116	C	G	MYD88	intronic	NA	NA	0.0028
77	112	Case	3	38182244	C	T	MYD88	intronic	NA	NA	0.0009

77	112	Case	4	106157368	C	-	TET2	exonic	L757fs	COSM4383837	0.0679
77	112	Case	4	106164871	G	T	TET2	exonic	E1247X	NA	0.0099
77	112	Case	7	50468182	G	T	IKZF1	exonic	D473Y	NA	0.0050
77	112	Case	7	101844954	G	A	CUX1	exonic	G793R	NA	0.0045
77	112	Case	X	39932217	C	A	BCOR	exonic	G794G	NA	0.0006
78	112	Cntl 2	2	25467448	C	T	DNMT3A	exonic	G543D	NA	0.0065
78	112	Cntl 2	2	25497888	C	A	DNMT3A	exonic	R187S	NA	0.0018
78	112	Cntl 2	3	128205780	T	C	GATA2	exonic	N32S	NA	0.0013
78	112	Cntl 2	4	106157845	C	T	TET2	exonic	Q916X	COSM43417	0.0032
79	119	Case	2	25463278	GCA	-	DNMT3A	exonic	738_739 del	NA	0.0028
79	119	Case	4	106197036	T	A	TET2	exonic	L1790H	NA	0.0003
79	119	Case	7	101921284	A	T	CUX1	exonic	D543V	NA	0.0012
79	119	Case	9	21971132	C	T	CDKN2A	exonic	A76T	COSM13712	0.0011
79	119	Case	X	15827426	G	T	ZRSR2	exonic	C181F	COSM4385283	0.0014
79	119	Case	X	53423497	G	T	SMC1A	exonic	A868D	NA	0.0020
80	119	Cntl 2	12	12037480	G	T	ETV6	exonic	V371L	NA	0.0008
80	119	Cntl 2	2	25469946	G	A	DNMT3A	exonic	R366C	NA	0.0012
80	119	Cntl 2	2	25470498	G	A	DNMT3A	exonic	R326C	COSM4169721	0.0087
80	119	Cntl 2	4	153247240	A	T	FBXW7	exonic	F521Y	NA	0.0008
80	119	Cntl 2	7	101877431	G	T	CUX1	exonic	G1178V	NA	0.0007
80	119	Cntl 2	9	21968310	C	T	CDKN2A	intronic	NA	NA	0.0013
80	119	Cntl 2	X	44942757	G	C	KDM6A	exonic	V1113L	COSM4168304	0.0021
81	119	Cntl 1	2	25463241	A	C	DNMT3A	exonic	F751C	NA	0.0040
81	119	Cntl 1	2	25464449	-	CGGA	DNMT3A	exonic	R688fs	NA	0.0045
81	119	Cntl 1	2	25464451	G	T	DNMT3A	exonic	R688S	COSM1583091	0.0024
81	119	Cntl 1	2	25467128	A	G	DNMT3A	exonic	C583R	NA	0.0009
81	119	Cntl 1	2	25469137	C	-	DNMT3A	exonic	V441fs	NA	0.0028
81	119	Cntl 1	2	25470498	G	A	DNMT3A	exonic	R326C	COSM4169721	0.0205
81	119	Cntl 1	20	31022701	G	T	ASXL1	exonic	S729I	NA	0.0007
81	119	Cntl 1	21	36421234	G	A	RUNX1	UTR5	NA	NA	0.0003
81	119	Cntl 1	3	38181992	G	T	MYD88	exonic	V206L	NA	0.0012
81	119	Cntl 1	4	106156906	A	T	TET2	exonic	K603X	NA	0.0009
81	119	Cntl 1	7	101877440	C	T	CUX1	exonic	P1181L	NA	0.0008
81	119	Cntl 1	X	39932913	C	A	BCOR	exonic	S562S	NA	0.0014
81	119	Cntl 1	X	39933669	A	T	BCOR	exonic	S310R	NA	0.0009
81	119	Cntl 1	X	129149555	C	A	BCORL1	exonic	S936Y	NA	0.0008
82	101	Cntl 1	2	25457191	C	T	DNMT3A	exonic	R899H	COSM1583134	0.0034
82	101	Cntl 1	2	25458628	G	A	DNMT3A	exonic	P849S	NA	0.0007
82	101	Cntl 1	2	25463295	T	C	DNMT3A	exonic	E733G	COSM4169943	0.1271
82	101	Cntl 1	2	25468156	G	C	DNMT3A	exonic	P507R	NA	0.0095
82	101	Cntl 1	2	25469139	C	T	DNMT3A	exonic	W440X	NA	0.0182
82	101	Cntl 1	2	25470575	A	G	DNMT3A	exonic	L300P	COSM1019243	0.0005
82	101	Cntl 1	2	25470986	C	-	DNMT3A	exonic	A259fs	NA	0.0040
82	101	Cntl 1	2	25472637	A	T	DNMT3A	intronic	NA	NA	0.0010
82	101	Cntl 1	3	128202761	C	T	GATA2	exonic	G320D	COSM249854	0.0008
82	101	Cntl 1	4	106158054	T	A	TET2	exonic	P985P	NA	0.0008
82	101	Cntl 1	4	106197285	T	C	TET2	exonic	I1873T	COSM41741	0.1128
82	101	Cntl 1	9	5073770	G	T	JAK2	exonic	V617F	COSM12600	0.0191
82	101	Cntl 1	9	139390577	G	T	NOTCH1	exonic	S2538R	NA	0.0013

82	101	Cntl 1	9	139399629	C	T	NOTCH1	intronic	NA	NA	0.0017
82	101	Cntl 1	X	129171449	C	T	BCORL1	exonic	I1471I	NA	0.0010
83	101	Cntl 2									
84	101	Case	12	12006492	G	T	ETV6	exonic	E154X	COSM5478015	0.0021
84	101	Case	12	25398281	C	T	KRAS	exonic	G13D	COSM532	0.0304
84	101	Case	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.0847
84	101	Case	2	25469528	-	G	DNMT3A	exonic	F414fs	NA	0.0357
84	101	Case	2	25470484	C	T	DNMT3A	exonic	W330X	COSM249799	0.0853
84	101	Case	7	101837219	G	C	CUX1	intronic	NA	NA	0.0005
84	101	Case	8	117875424	G	T	RAD21	exonic	Y73X	NA	0.0014
84	101	Case	9	133738512	T	C	ABL1	intronic	NA	NA	0.0002
85	107	Cntl 1	12	25398277	T	C	KRAS	exonic	V14V	NA	0.0006
85	107	Cntl 1	21	36252957	G	C	RUNX1	exonic	Q38E	NA	0.0005
85	107	Cntl 1	4	106196561	C	T	TET2	exonic	Q1632X	COSM3719314	0.0007
85	107	Cntl 1	9	133748402	G	C	ABL1	exonic	E355Q	NA	0.0027
86	107	Case	11	119148875	G	T	CBL	splicing	NA	NA	0.0017
86	107	Case	4	106156981	G	T	TET2	exonic	E628X	NA	0.0012
86	107	Case	4	106157404	C	T	TET2	exonic	Q769X	NA	0.0018
86	107	Case	4	106157788	C	T	TET2	exonic	Q897X	NA	0.1586
86	107	Case	4	106164022	GA	-	TET2	exonic	E1178fs	NA	0.0114
86	107	Case	4	106164866	A	G	TET2	exonic	Y1245C	NA	0.0008
86	107	Case	9	5073770	G	T	JAK2	exonic	V617F	COSM12600	0.0073
86	107	Case	X	129148441	C	A	BCORL1	exonic	Q565K	NA	0.0012
87	107	Cntl 2	2	25462089	A	T	DNMT3A	intronic	NA	NA	0.0047
87	107	Cntl 2	2	25467468	G	T	DNMT3A	exonic	Y536X	NA	0.0036
87	107	Cntl 2	9	133748334	G	A	ABL1	exonic	R332Q	NA	0.0004
87	107	Cntl 2	X	123215326	A	C	STAG2	exonic	T958P	NA	0.0011
88	113	Case	2	25463275	C	T	DNMT3A	exonic	D740N	NA	0.0009
88	113	Case	2	25463400	G	A	DNMT3A	intronic	NA	NA	0.0013
88	113	Case	20	31022289	C	T	ASXL1	exonic	Q592X	COSM96400	0.0010
88	113	Case	8	117864237	G	A	RAD21	exonic	Q474X	COSM13911	0.0020
88	113	Case	X	44922695	G	A	KDM6A	exonic	R519Q	NA	0.0028
89	113	Cntl 1	2	25463579	G	C	DNMT3A	exonic	F701L	NA	0.0061
89	113	Cntl 1	2	25470535	C	T	DNMT3A	exonic	W313X	COSM3372726	0.0017
89	113	Cntl 1	4	106155643	C	G	TET2	exonic	L182V	NA	0.0004
89	113	Cntl 1	4	106157986	C	T	TET2	exonic	Q963X	COSM100070	0.0011
89	113	Cntl 1	X	129148453	C	T	BCORL1	exonic	P569S	NA	0.0009
90	113	Cntl 2	11	32413690	G	A	WT1	intronic	NA	NA	0.0122
90	113	Cntl 2	17	74733079	C	G	SRSF2	exonic	R55P	NA	0.0025
90	113	Cntl 2	2	25458648	T	C	DNMT3A	exonic	Q842R	NA	0.0029
90	113	Cntl 2	2	25463574	A	G	DNMT3A	exonic	L703P	NA	0.0017
90	113	Cntl 2	2	25464468	A	C	DNMT3A	exonic	M682R	NA	0.0029
90	113	Cntl 2	4	55593431	G	A	KIT	exonic	V530I	NA	0.0037
90	113	Cntl 2	7	50455144	G	T	IKZF1	exonic	G231C	NA	0.0023
91	111	Cntl 1	17	7577566	T	C	TP53	exonic	N239D	COSM10777	0.0006
91	111	Cntl 1	2	25458696	T	C	DNMT3A	splicing	NA	NA	0.0376
91	111	Cntl 1	2	25459837	G	-	DNMT3A	exonic	Q816fs	NA	0.0031
91	111	Cntl 1	2	25463229	A	G	DNMT3A	exonic	F755S	COSM2911748	0.0006
91	111	Cntl 1	2	25463277	T	G	DNMT3A	exonic	H739P	NA	0.0031

91	111	Cntl 1	2	25468936	G	C	DNMT3A	intronic	NA	NA	0.0033
91	111	Cntl 1	2	25470029	T	C	DNMT3A	splicing	NA	NA	0.0026
91	111	Cntl 1	20	31022687	G	T	ASXL1	exonic	L724L	NA	0.0012
91	111	Cntl 1	7	101877421	A	T	CUX1	exonic	S1175C	NA	0.0010
91	111	Cntl 1	7	148515071	A	T	EZH2	exonic	S380T	NA	0.0012
91	111	Cntl 1	X	129146912	T	A	BCORL1	intronic	NA	NA	0.0010
91	111	Cntl 1	X	129147527	C	G	BCORL1	exonic	P260R	NA	0.0006
92	111	Cntl 2	11	119149284	T	C	CBL	exonic	V431A	NA	0.0011
92	111	Cntl 2	2	25463241	A	G	DNMT3A	exonic	F751S	NA	0.0820
92	111	Cntl 2	2	25463271	G	A	DNMT3A	exonic	A741V	COSM166528	0.0007
92	111	Cntl 2	4	106196237	C	T	TET2	exonic	Q1524X	NA	0.0017
92	111	Cntl 2	7	101755089	G	T	CUX1	intronic	NA	NA	0.0008
93	111	Case	2	25469598	G	T	DNMT3A	exonic	S390R	NA	0.0019
93	111	Case	21	36252861	A	T	RUNX1	exonic	S167R	COSM1318811	0.0013
93	111	Case	4	106157848	C	T	TET2	exonic	Q917X	COSM5487354	0.0129
93	111	Case	4	106164075	TGCTAAGTGGGTAAGTG	-	TET2	exonic	I1195fs	NA	0.0029
93	111	Case	4	106180865	G	A	TET2	exonic	C1298Y	COSM87138	0.0011
93	111	Case	4	106180926	G	A	TET2	exonic	E1318E	NA	0.2099
93	111	Case	4	106190816	G	T	TET2	exonic	G1365V	NA	0.0057
93	111	Case	4	106197373	C	G	TET2	exonic	Y1902X	NA	0.0008
93	111	Case	9	21971240	G	A	CDKN2A	UTR5	NA	NA	0.0023
93	111	Case	9	139391190	G	A	NOTCH1	exonic	P2334L	NA	0.0014
93	111	Case	9	139391207	C	A	NOTCH1	exonic	G2328G	NA	0.0014
93	111	Case	X	133559310	G	A	PHF6	exonic	V350I	NA	0.0013
94	115	Cntl 2	2	25457242	C	T	DNMT3A	exonic	R882H	COSM52944	0.0178
94	115	Cntl 2	2	25458588	G	A	DNMT3A	exonic	T862I	NA	0.0010
94	115	Cntl 2	2	25459913	G	C	DNMT3A	intronic	NA	NA	0.0005
94	115	Cntl 2	2	25463299	A	G	DNMT3A	exonic	F732L	COSM4383544	0.0185
94	115	Cntl 2	2	25463642	C	G	DNMT3A	intronic	NA	NA	0.0273
94	115	Cntl 2	2	25470542	A	C	DNMT3A	exonic	V311G	NA	0.0006
95	115	Case	15	90631934	C	T	IDH2	exonic	R140Q	COSM41590	0.0384
95	115	Case	17	7578190	T	C	TP53	exonic	Y220C	COSM10758	0.0026
95	115	Case	2	25457252	T	C	DNMT3A	exonic	N879D	COSM1583135	0.0047
95	115	Case	2	25470029	T	C	DNMT3A	splicing	NA	NA	0.0013
95	115	Case	2	198266724	G	A	SF3B1	exonic	R736R	NA	0.0020
95	115	Case	4	106162549	C	T	TET2	exonic	P1155S	NA	0.0015
96	115	Cntl 1	2	25457243	G	A	DNMT3A	exonic	R882C	COSM53042	0.0011
96	115	Cntl 1	4	106197354	G	C	TET2	exonic	R1896T	COSM4766171	0.0010
97	106	Cntl 1	17	7578523	T	G	TP53	exonic	Q136P	COSM45089	0.0007
97	106	Cntl 1	2	25467408	C	T	DNMT3A	splicing	NA	COSM3720632	0.0089
97	106	Cntl 1	20	31024028	G	C	ASXL1	exonic	R1171S	NA	0.0007
97	106	Cntl 1	4	106164039	T	C	TET2	exonic	L1153P	NA	0.0008
97	106	Cntl 1	4	106194038	A	C	TET2	exonic	K1500N	NA	0.0082
97	106	Cntl 1	7	148506461	C	G	EZH2	exonic	R684P	NA	0.0016
97	106	Cntl 1	9	133738480	T	G	ABL1	intronic	NA	NA	0.0009
98	106	Cntl 2	2	25471058	C	A	DNMT3A	exonic	E235X	NA	0.0050
98	106	Cntl 2	20	31023618	C	A	ASXL1	exonic	P1035T	NA	0.0004

98	106	Cntl 2	7	101891797	C	T	CUX1	exonic	P1331P	NA	0.0019
99	106	Case	2	25463536	C	T	DNMT3A	exonic	V716I	COSM249137	0.0027
99	106	Case	2	25470535	C	T	DNMT3A	exonic	W313X	COSM3372726	0.0020
99	106	Case	4	106197398	A	C	TET2	exonic	K1911Q	NA	0.0016
99	106	Case	7	148511163	A	G	EZH2	exonic	L580P	NA	0.0006
99	106	Case	X	39931967	C	T	BCOR	exonic	V878I	COSM4665535	0.0018
100	102	Cntl 1	4	55561755	C	A	KIT	exonic	R49S	NA	0.0020
100	102	Cntl 1	4	153247246	T	C	FBXW7	exonic	Y519C	COSM27054	0.0005
100	102	Cntl 1	X	44897016	G	-	KDM6A	intronic	NA	NA	0.0051
100	102	Cntl 1	X	76888754	C	A	ATRX	exonic	G1692V	NA	0.0009
101	102	Case	11	119148906	T	C	CBL	exonic	S376P	NA	0.0009
101	102	Case	11	119148919	T	C	CBL	exonic	L380P	COSM34055	0.0027
101	102	Case	11	119148982	G	A	CBL	exonic	C401Y	COSM87284	0.0020
101	102	Case	11	119149247	T	C	CBL	exonic	C419R	COSM41790	0.0023
101	102	Case	7	101821814	G	T	CUX1	exonic	E298D	NA	0.0008
101	102	Case	X	129149196	G	T	BCORL1	exonic	R816R	NA	0.0014
102	102	Cntl 2	2	25463239	A	G	DNMT3A	exonic	F752L	COSM133131	0.0022
102	102	Cntl 2	4	106156773	C	T	TET2	exonic	H558H	NA	0.0009
102	102	Cntl 2	4	106162585	A	G	TET2	exonic	R1167G	NA	0.0010
102	102	Cntl 2	7	148523690	C	G	EZH2	exonic	A255P	NA	0.0008
102	102	Cntl 2	X	76890155	T	A	ATRX	exonic	K1580I	NA	0.0009
103	108	Case	20	31023774	T	A	ASXL1	exonic	Y1087N	NA	0.0005
103	108	Case	9	139397730	G	T	NOTCH1	exonic	Q1691K	NA	0.0011
103	108	Case	X	39933370	G	T	BCOR	exonic	A410D	NA	0.0010
103	108	Case	X	53423476	T	C	SMC1A	exonic	N875S	NA	0.0014
103	108	Case	X	129146912	T	A	BCORL1	intronic	NA	NA	0.0009
103	108	Case	X	129147701	A	T	BCORL1	exonic	Q318L	NA	0.0075
104	108	Cntl 2	19	33792372	G	C	CEBPA	exonic	L317V	NA	0.0007
104	108	Cntl 2	2	25471187	C	T	DNMT3A	intronic	NA	NA	0.0008
104	108	Cntl 2	4	106157528	A	T	TET2	exonic	Q810L	NA	0.0009
104	108	Cntl 2	X	44929425	C	A	KDM6A	exonic	T842N	NA	0.0014
105	108	Cntl 1	11	118343176	T	C	KMT2A	exonic	Y434Y	NA	0.0006
105	108	Cntl 1	4	106158252	G	T	TET2	exonic	Q1051H	NA	0.0010

Supplementary Table 3. Droplet digital PCR (ddPCR) validation experiments for 61 clonal mutations identified in 37 individuals. There were 37 mutations detected and validated in individuals with only a single banked sample. There were 12 mutations detected in individuals with two banked samples, which were both used for ddPCR validation. The variant allele fraction (VAF) for each mutation identified by error-corrected sequencing (ECS) was reported alongside the VAF measured by ddPCR. For each identified mutation, a separate sample where that mutation was not observed by ECS was selected as a negative control.

			Collection 1			Collection 2			
Participant Number	Gene	Amino Acid Change	ECS VAF Replicate 1	ECS VAF Replicate 2	ddPCR VAF	ECS VAF Replicate 1	ECS VAF Replicate 2	ddPCR VAF	Negative Control VAF
3	TET2	L1322fs	0.0040	0.0037	0.0041	0.0117	0.0135	0.0113	0.000000
4	KIT	L46fs	0.0000	0.0000	0.0000	0.0022	0.0022	0.0017	0.000000
5	DNMT3A	R635W	0.0020	0.0010	0.0027	0.0018	0.0012	0.0019	0.000000
9	DNMT3A	P904L	0.0042	0.0049	0.0034	NA	NA	NA	0.000000
10	DNMT3A	C487fs	0.0000	0.0000	0.0016	0.0055	0.0037	0.0044	0.000000
17	DNMT3A	e15spAins	0.0040	0.0041	0.0041	0.0101	0.0100	0.0094	0.000000
18	DNMT3A	I780T	0.0014	0.0020	0.0020	NA	NA	NA	0.000000
23	DNMT3A	R882H	0.0034	0.0034	0.0042	NA	NA	NA	0.000051
25	DNMT3A	R882H	0.0032	0.0010	0.0010	0.0022	0.0028	0.0011	0.000000
26	DNMT3A	W860R	0.0015	0.0012	0.0013	0.0003	0.0010	0.0003	0.000000
30	DNMT3A	R882H	0.0039	0.0032	0.0061	0.0180	0.0150	0.0158	0.000000
32	DNMT3A	S714C	0.0053	0.0098	0.0062	0.0057	0.0073	0.0078	0.000000
33	DNMT3A	e15spCdel	0.0030	0.0000	0.0018	0.0032	0.0032	0.0026	0.000000
40	DNMT3A	R326C	0.0000	0.0000	0.0002	0.0021	0.0034	0.0022	0.000082
42	TET2	L1276fs	0.0057	0.0057	0.0061	0.0000	0.0000	0.0013	0.000000
46	DNMT3A	W860R	NA	NA	NA	0.0024	0.0024	0.0022	0.000000
46	TET2	e3splice	NA	NA	NA	0.0263	0.0202	0.0216	0.000054
47	DNMT3A	L504fs	NA	NA	NA	0.0172	0.0181	0.0142	0.000000
50	JAK2	V617F	0.0783	0.0835	0.0871	NA	NA	NA	0.000000
51	DNMT3A	R882C	0.0700	0.0701	0.0761	NA	NA	NA	0.000000
52	JAK2	V617F	0.0260	0.0295	0.0299	NA	NA	NA	0.000000
52	DNMT3A	R882C	0.0030	0.0031	0.0025	NA	NA	NA	0.000000
52	DNMT3A	P385fs	0.0084	0.0079	0.0068	NA	NA	NA	0.000000
56	DNMT3A	P904L	0.0137	0.0169	0.0154	NA	NA	NA	0.000000
56	JAK2	V617F	0.0227	0.0263	0.0240	NA	NA	NA	0.000000
59	DNMT3A	W860R	0.0083	0.0091	0.0081	NA	NA	NA	0.000000
61	DNMT3A	R882H	0.2957	0.2860	0.3117	NA	NA	NA	0.000000
65	DNMT3A	W860R	0.0011	0.0015	0.0011	NA	NA	NA	0.000000
65	DNMT3A	N757fs	0.0040	0.0058	0.0051	NA	NA	NA	0.000000
66	DNMT3A	I780T	0.0189	0.0246	0.0239	NA	NA	NA	0.000000
66	TET2	P463fs	0.0289	0.0257	0.0312	NA	NA	NA	0.000000
71	DNMT3A	W860R	0.0012	0.0007	0.0010	NA	NA	NA	0.000000
72	DNMT3A	I780T	0.0028	0.0013	0.0021	NA	NA	NA	0.000000
72	DNMT3A	R326C	0.0010	0.0033	0.0024	NA	NA	NA	0.000082
72	DNMT3A	R882H	0.0025	0.0029	0.0033	NA	NA	NA	0.000051
75	DNMT3A	G543A	0.0008	0.0009	0.0017	NA	NA	NA	0.000000
75	DNMT3A	I780T	0.0008	0.0010	0.0007	NA	NA	NA	0.000000
75	DNMT3A	E733delInX	0.0046	0.0027	0.0032	NA	NA	NA	0.000000
77	DNMT3A	R882H	0.3350	0.3211	0.3536	NA	NA	NA	0.000051

77	TET2	L757fs	0.0689	0.0668	0.0705	NA	NA	NA	0.000000
79	DNMT3A	738_739del	0.0035	0.0021	0.0030	NA	NA	NA	0.000000
80	DNMT3A	R326C	0.0106	0.0068	0.0080	NA	NA	NA	0.000082
81	DNMT3A	R326C	0.0196	0.0213	0.0223	NA	NA	NA	0.000082
82	JAK2	V617F	0.0198	0.0183	0.0173	NA	NA	NA	0.000000
84	DNMT3A	R882H	0.0910	0.0784	0.0881	NA	NA	NA	0.000051
86	JAK2	V617F	0.0063	0.0083	0.0065	NA	NA	NA	0.000000
86	TET2	E1178fs	0.0097	0.0131	0.0101	NA	NA	NA	0.000000
94	DNMT3A	R882H	0.0181	0.0175	0.0164	NA	NA	NA	0.000051
96	DNMT3A	R882C	0.0014	0.0008	0.0018	NA	NA	NA	0.000000