Supplemental Methods and Materials

Patients

A total of 799 patients with various myeloid neoplasms (MNs) (n = 575), BMFs (n = 105) and other hematologic disorders (n = 119) were screened. All samples were obtained after written informed consent, according to protocols approved by the Institutional Review Board of participating institutions. The patients with myeloid neoplasm consisted of MDS (n = 422), acute myeloid leukemia (AML) (n = 98), and MDS/myeloproliferative neoplasms (MPN) (n = 55). Most (78/98, 80%) AML patients had secondary (post-MDS) disease. The BMF cohorts were aplastic anemia (AA) (n = 47), paroxysmal nocturnal hemoglobinuria (PNH) (n = 40), and pure red cell aplasia (PRCA) (n = 18). The other hematologic disorders were large granular lymphocytic leukemia (n = 55) and idiopathic cytopenia of undetermined significance (n = 20). We sequenced all patients for the presence of *SAMD9/SAMD9L* variants. Paired disease and normal GL DNA were obtained from 220 MN patients for whole exome sequencing (WES). GL DNA was obtained from either buccal mucosa or CD3 positive T cells which were purified from peripheral blood with or without prior culture in the presence of PHA and IL-2[1]. Disease DNA was extracted from bone marrow or peripheral blood. 579 patients were evaluated by targeted capture sequencing. We used Broad Institute's Genome Aggregation Database (gnomAD) as healthy controls (n = 138,632) which included 123,136 WES and 15,496 whole-genome sequences from unrelated individuals[2]. After comparing ethnicities between gnomAD and our cohort[2,3], we matched healthy controls to patients by ethnicities (Supplemental Figure 3).

Whole exome sequencing

WES was performed as previously described[1,4]. Paired disease and normal GL DNAs were used. Whole-exome capture was accomplished through hybridization of sonicated genomic DNA to a bait cDNA library synthesized on magnetic beads (SureSelect Human All Exon 50Mb or V4 kit, Agilent Technologies). Captured targets were subjected to massively parallel sequencing using a HiSeq 2000 (Illumina) according to the standard protocol for 100-bp paired-end reads. Subsequent validation and confirmatory sequencing are described below. Briefly, sequencing reads were aligned to the human genome (hg19) by a Burrows-Wheeler aligner (http://bio-bwa.sourceforge.net/). We used a GATK pipeline to extract candidate variants/polymorphisms and to remove sequencing errors. Validations were performed by Sanger or PCR amplicon sequencing[4].

Targeted Capture Sequencing

Targeted capture sequencing was performed using a TruSeq Custom Amplicon or Nextera Rapid capture custom enrichment kit (Illumina) as previously described[4,5]. The targeted 46 genes were captured (Supplemental Table 2 and 3). Sequencing libraries were generated according to an Illumina paired-end library protocol. The enriched targets were subjected to massive sequencing using HiSeq 2000 or MiSeq sequencer (Illumina), with sufficient read coverage (Supplemental Figure 2). Variants were annotated using ANNOVAR[6] and filtered by removing: i) synonymous single nucleotide variants; ii) variants only present in unidirectional reads; iii) variants in repetitive genomic regions. Only variants with minimum depth of 20 and with 5 positive, high quality reads, were considered. Variant allelic frequencies were adjusted according to zygosity and copy number based on single nucleotide polymorphism array results[5]. Finally, mapping errors were removed by visual inspection with the Integral Genomics Viewer. Validation by Sanger sequencing or PCR amplicon sequencing was performed as previously described[5].

Criteria of rare variants and pathogenic missense variants

We defined “rare variants” of *SAMD9/SAMD9L* genes as those present in <0.1% of ethnically-matched healthy controls (Supplemental Figure 3). To predict functional effects of specific *SAMD9* missense variants, we focused on *SAMD9* germline variants reported in previous papers[7,8] or public databases of healthy donors. 39 variants were identified, 23 out of 39 were deemed “truly pathogenic” variants by confirming that there was a significant phenotype using a functional assay and by examining familial disease phenotype co-segregations (Supplemental Table 5). ROC curves of 8 different algorithms[9-13] were created (Supplemental figure 4), and Areas Under the Curves (AUC) were compared between them (Supplemental Table 6). We set a strict cut-off to discover missense variants with high probabilities of pathogenesis, even if it reduces the sensitivity. The top 5 algorithms in terms of greatest AUC were chosen and variants with $\geq$3 positive scores out of the top 5 algorithms were defined as “Pathogenic”. Applying this criteria to 39 variants already confirmed to be pathogenic or not yielded 9 as positive and 7 as truly pathogenic (Supplemental figure 5). Given that 23 were truly pathogenic and 16 were not, sensitivity and specificity were 30% (7/(7+16)) and 88% (14/(14+2)), respectively.

Metaphase cytogenetics

Chromosome preparations were G-banded using trypsin and Giemsa, and karyotypes were described in 799 patients according to the International System for Human Cytogenetic Nomenclature[14].

Single-nucleotide polymorphism array analysis

Single-nucleotide polymorphism (SNP) array karyotyping for confirming metaphase cytogenetics and detecting copy-number neutral loss of heterozygosity was performed as previously described[15,16]. Briefly, Affymetrix 250K and 6.0 SNP arrays were used to evaluate copy number and loss of heterozygosity. Using our internal and a publicly available database (http://dgv.tcag.ca/dgv/app/home), the screening algorithm validated each lesion as somatic. Non-somatic lesions were excluded from further analysis. Affected genomic positions in each lesion were visualized and extracted using CNAG (v3.0) or Genotyping Console (Affymetrix)[17,18].

Mutagenesis and constructs

A plasmid encoding N-terminal FLAG-tagged human SAMD9 with the tetracycline-inducible system was used as described previously[19]. Plasmids encoding five SAMD9 variants (Thr205Pro, Ile247Thr, Ile268Thr, Asp550Val, and Leu574Pro) were generated with a standard site-directed mutagenesis technique with use of wild-type (WT) SAMD9-expressing vector as a template. We also created a vector encoding N-terminal TagRFP-tagged human SAMD9L by inserting the TagRFP sequence (derived from pTagRFP-C [Evrogen, Moscow, Russia]) and human SAMD9L cDNA sequence, and deleting the SAMD9 sequence. Plasmids encoding 9 SAMD9L variants (Leu50Ser, Glu220Gly, Cys228Tyr, Gly235Ser, Gly247Ala, Trp333Cys, Trp517Arg, His880Glu, and Leu1323fs) were generated with a site-directed mutagenesis technique.

Inducible stably transfected HEK293 cells

HEK293 cells were purchased from the American Type Culture Collection (ATCC CRL-1573). Mycoplasma infection was excluded through the standard indirect DNA staining method. HEK293 cell lines stably expressing each FLAG-SAMD9 and TagRFP-SAMD9L proteins (wild type, mutant, or empty vector) in the presence of doxycycline (1 μg/mL) were established according to the manufacturer's protocol[7,19]. Cells were maintained in DMEM supplemented with 10% FBS in a humidified incubator at 37°C and 5% CO2.

Intracellular localization analysis

Inducible stable HEK293 cells were grown on glass-bottom dishes (Greiner bio-one). Forty-eight hours after induction, cells were fixed and permeabilized by incubation in cold methanol at -20°C for 10 min. Nuclei were stained with Hoechst 33342 (Dojindo). Images were obtained by confocal laser scanning microscopy FV1000D (Olympus).

Cell proliferation assays

For cell growth assays, inducible stable HEK293 cells, were seeded into 96-well plate with about 5% confluence in 200 µL of culture medium with or without 1 µg/mL doxycycline. The degree of confluence was quantified every 3 hours using an IncuCyte ZOOM time-lapse microscope (Essen BioScience). Growth curve data are representative of three independent assays that were performed in triplicate.

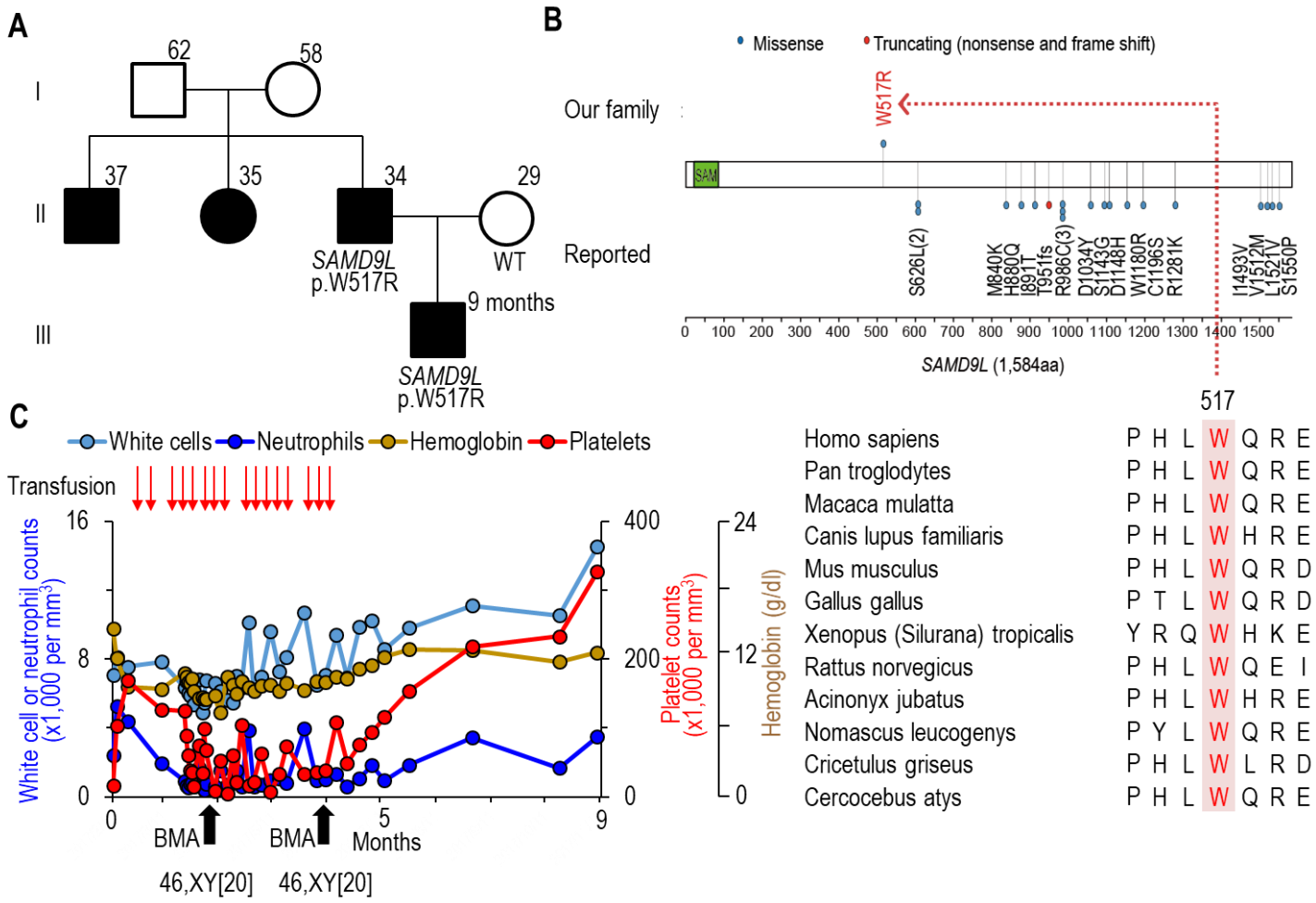
Statistical analyses

Proportions were compared using two-sided Fisher exact tests using R.

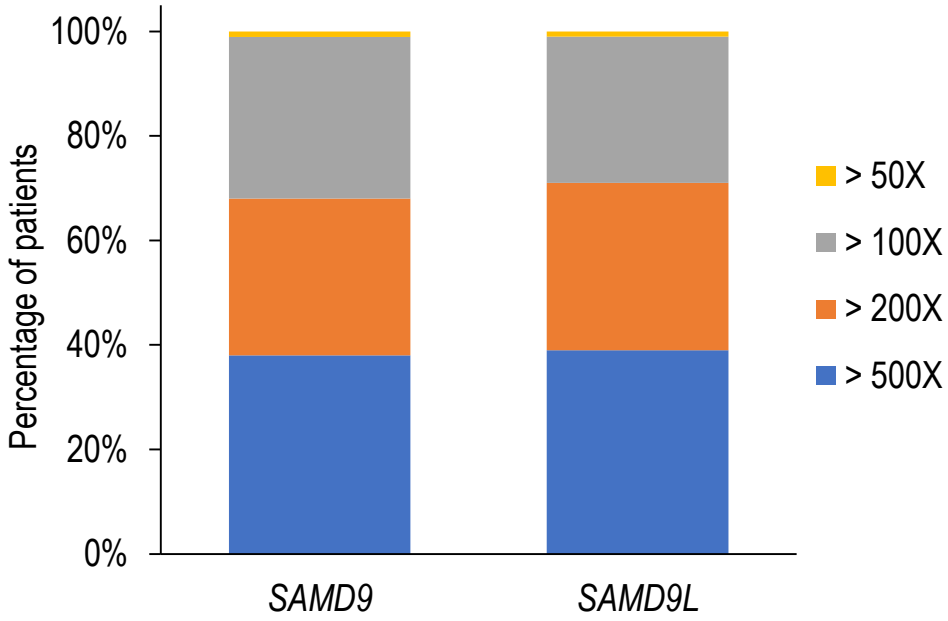
References

1. Makishima H, Yoshida K, Nguyen N, et al. Somatic SETBP1 mutations in myeloid malignancies. *Nature Genetics*. 2013;45(8):942-946.
2. Lek M, Karczewski KJ, Minikel EV, et al. Analysis of protein-coding genetic variation in 60,706 humans. *Nature*. 2016;536(7616):285-291.
3. Nazha A, Al-Issa K, Przychodzen B, et al. Differences in genomic patterns and clinical outcomes between African-American and White patients with myelodysplastic syndromes. *Blood Cancer J*. 2017;7(9):e602.
4. Makishima H, Yoshizato T, Yoshida K, et al. Dynamics of clonal evolution in myelodysplastic syndromes. *Nat Genet*. 2017;49(2):204-212.
5. Hirsch CM, Przychodzen BP, Radivoyevitch T, et al. Molecular features of early onset adult myelodysplastic syndrome. *Haematologica*. 2017.
6. Wang K, Li M, Hakonarson H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res*. 2010;38(16):e164.
7. Narumi S, Amano N, Ishii T, et al. SAMD9 mutations cause a novel multisystem disorder, MIRAGE syndrome, and are associated with loss of chromosome 7. *Nat Genet*. 2016;48(7):792-797.
8. Buonocore F, Kühnen P, Suntharalingham JP, et al. Somatic mutations and progressive monosomy modify SAMD9-related phenotypes in humans. *J Clin Invest*. 2017.
9. Dong C, Wei P, Jian X, et al. Comparison and integration of deleteriousness prediction methods for nonsynonymous SNVs in whole exome sequencing studies. *Hum Mol Genet*. 2015;24(8):2125-2137.
10. Adzhubei I, Jordan DM, Sunyaev SR. Predicting functional effect of human missense mutations using PolyPhen-2. *Curr Protoc Hum Genet*. 2013;Chapter 7:Unit7.20.
11. Schwarz JM, Rödelsperger C, Schuelke M, Seelow D. MutationTaster evaluates disease-causing potential of sequence alterations. *Nat Methods*. 2010;7(8):575-576.
12. Kumar P, Henikoff S, Ng PC. Predicting the effects of coding non-synonymous variants on protein function using the SIFT algorithm. *Nat Protoc*. 2009;4(7):1073-1081.
13. Choi Y, Sims GE, Murphy S, Miller JR, Chan AP. Predicting the functional effect of amino acid substitutions and indels. *PLoS One*. 2012;7(10):e46688.
14. Gonzalez Garcia JR, Meza-Espinoza JP. Use of the International System for Human Cytogenetic Nomenclature (ISCN). *Blood*. 2006;108(12):3952-3953; author reply 3953.
15. Thota S, Viny AD, Makishima H, et al. Genetic alterations of the cohesin complex genes in myeloid malignancies. *Blood*. 2014;124(11):1790-1798.
16. Nagata Y, Kontani K, Enami T, et al. Variegated RHOA mutations in adult T-cell leukemia/lymphoma. *Blood*. 2016;127(5):596-604.

17. Nannya Y, Sanada M, Nakazaki K, et al. A robust algorithm for copy number detection using high-density oligonucleotide single nucleotide polymorphism genotyping arrays. *Cancer Res*. 2005;65(14):6071-6079.
18. Yamamoto G, Nannya Y, Kato M, et al. Highly sensitive method for genomewide detection of allelic composition in nonpaired, primary tumor specimens by use of affymetrix single-nucleotide-polymorphism genotyping microarrays. *Am J Hum Genet*. 2007;81(1):114-126.
19. Shima H, Koehler K, Nomura Y, et al. Two patients with MIRAGE syndrome lacking haematological features: role of somatic second-site reversion SAMD9 mutations. *J Med Genet*. 2017.



Supplemental Figure 1. Characteristics of familial thrombocytopenia with SAMD9L variant. (A) A family tree identifying those with a SAMD9L variant (Trp517Arg) and their thrombocytopenic history (filled: thrombocytopenia; open: confirmed no thrombocytopenia). Ages are on the upper right of pedigree symbols. Paternity was confirmed by whole exome sequencing of patients' and parental germline DNAs. WT denotes wild type. (B) Graphical representation of SAMD9L protein. Functional sterile alpha motif (SAM) is depicted in green. Distribution of germline SAMD9L variants reported in pediatric MDS patients are shown in the lower panel. Amino acid alignment of SAMD9L proteins from different species shows evolutionarily conserved amino acids in red. Position of SAMD9L variants are indicated by a red arrow. (C) Clinical course of the 9-months-old patient with thrombocytopenia, including peripheral-blood counts, platelet transfusion times, and cytogenetics of marrow aspirates. After severe pancytopenia requiring transfusions for four months, this patient's cytopenias resolved spontaneously and he became transfusion-independent.



Supplemental Figure 2. Read coverage for *SAMD9* and *SAMD9L* in targeted capture sequencing. Shown are the percentages of patients with read coverages of more than 50×, 100×, 200× and 500× for *SAMD9 and SAMD9L*.

adjusted

Healthy control*

Population	# of healthy controls
European (Non-Finnish)	63,074
South Asian	15,381
East Asian	9,424
African	11,981
Latino	17,175
European (Finnish)	12,848
Ashkenazi Jewish	5,071
Other	3,222
Total	138,176

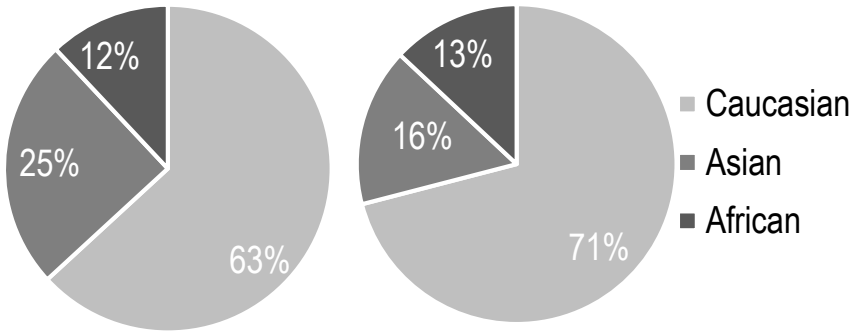
Ethnically-matched healthy control

Population	# of healthy controls
European (Non-Finnish)	63,074
South Asian	15,381
East Asian	9,424
African	11,981
Latino	0
European (Finnish)	0
Ashkenazi Jewish	0
Other	0
Total	99,860

Our cohorts

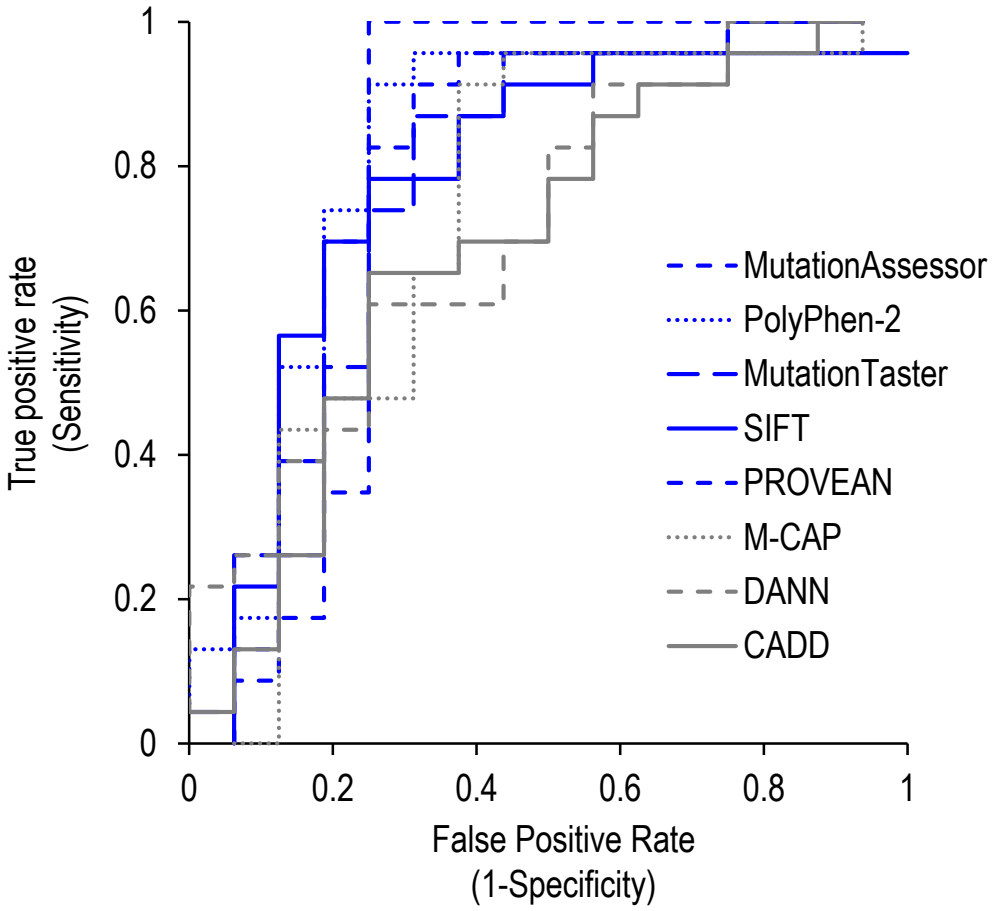
Population	# of patients
Caucasian	567
Asian	128
African	104
Total	799

* *SAMD9/SAMD9L* variants are available in the Genome Aggregation Database (gnomAD)[19,20].



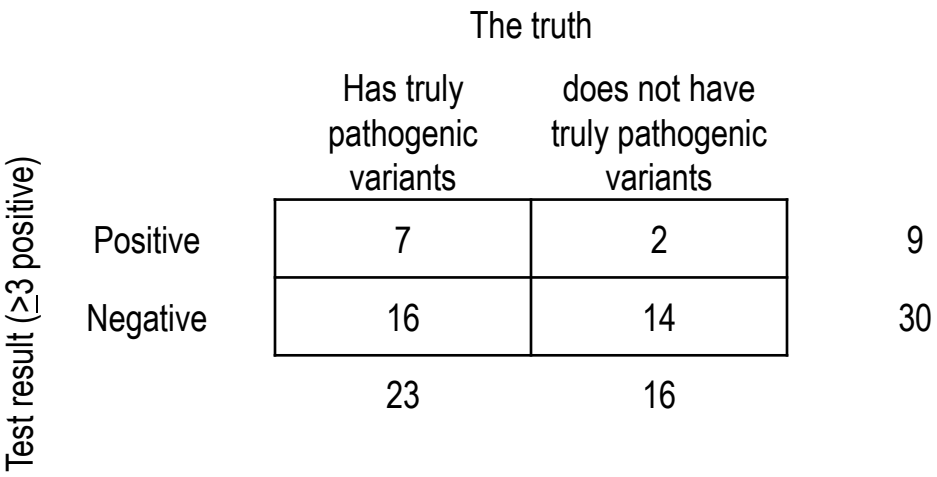
Supplemental Figure 3. Healthy controls were selected to have ethnicities that matched those of cases in our cohort.

We used Broad Institute's Genome Aggregation Database (gnomAD) to obtain ethnicity matched healthy controls (Center table) from a total of 138,176 subjects (Left table); to compare frequencies of germline *SAMD9/SAMD9L* variants in our sporadic adult MDS cohort (Right table) to these controls, ethnicities had to be matched. Thus, Latinos and Finns that were not included in our cohort were omitted, but Caucasians, Asians and African-Americans were included. Fractions of these races are depicted using pie charts.



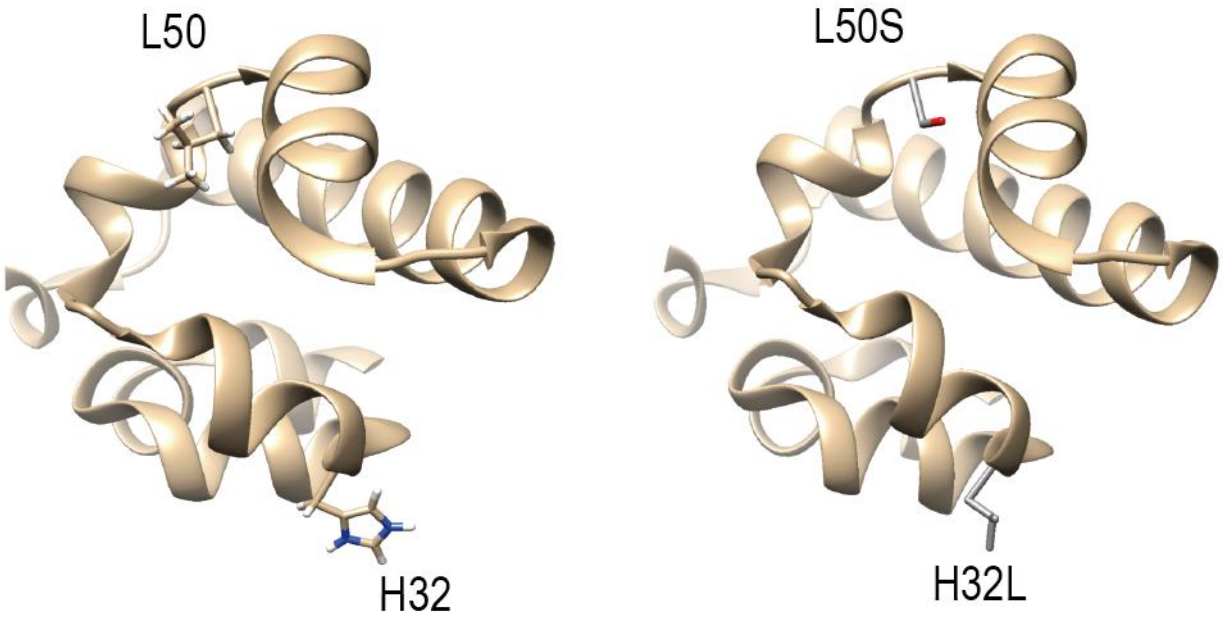
Supplemental Figure 4. Receiver Operating Characteristic curve for prediction algorithms for missense variants.

ROC curves of 8 different algorithms were created by using 39 variants which include 23 that were deemed "truly pathogenic" variants by confirming that there was a significant phenotype using a functional assay and by examining familial disease phenotype co-segregations. Blue line graphs depicted the top 5 algorithms in terms of greatest Area Under the Curve.

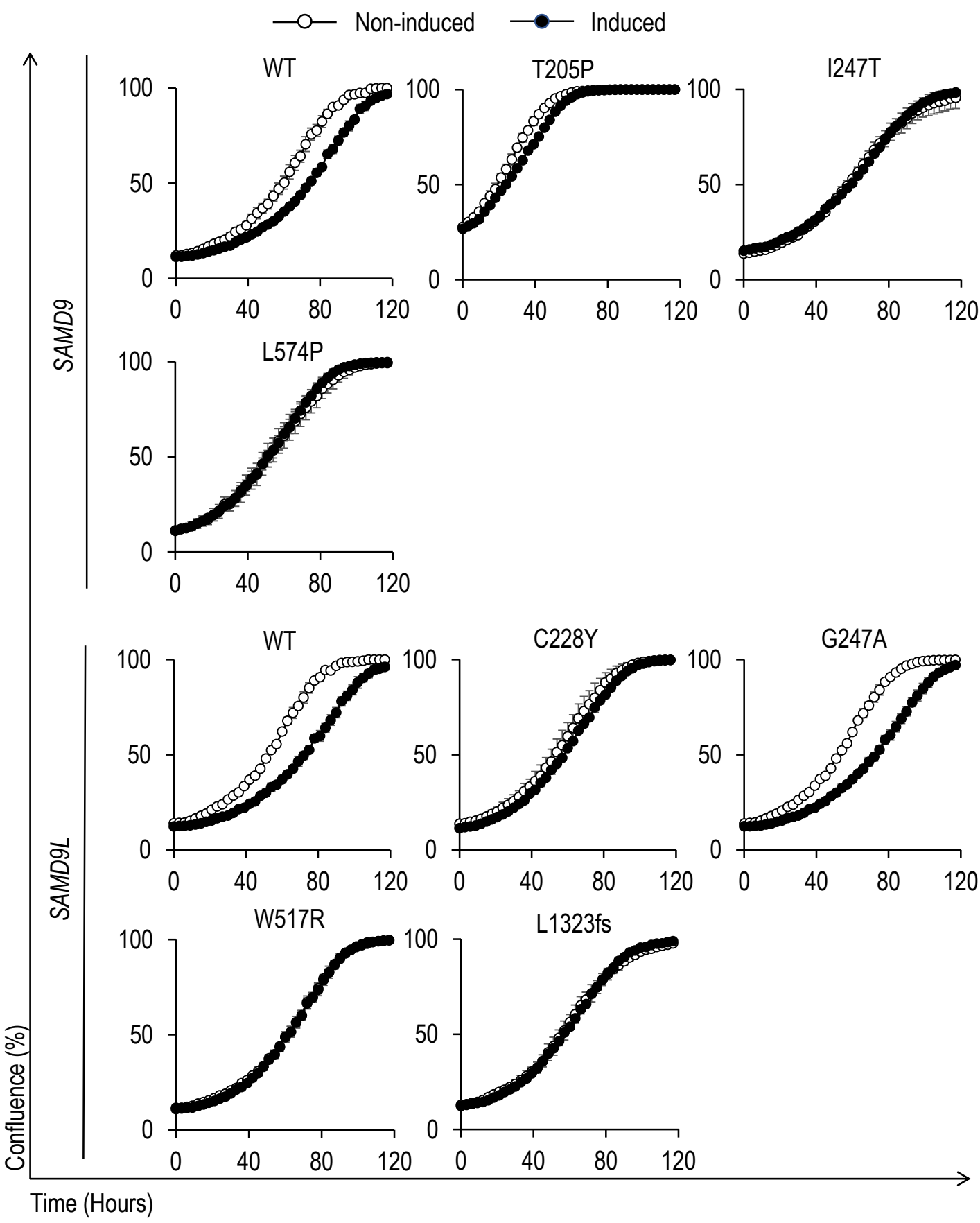


Supplemental Figure 5. Contingency table for prediction of SAMD9 missense variants

We set a strict cut-off (variants with ≥3 positive scores out of the top 5 algorithms in terms of greatest AUC) to discover missense variants with high possibilities of pathogenesis, even if it reduces the sensitivity. Applying this criteria to 39 variants already confirmed to be pathogenic or not yielded 9 as positive and 7 as truly pathogenic. Given that 23 were truly pathogenic and 16 were not, sensitivity and specificity were 30% (7/(7+16)) and 88% (14/(14+2)), respectively. Positive predict values and negative predict values were also 78% [7/(7+2)] and 47% [14/(16+14)].



Supplemental Figure 6. Three-dimensional structure of SAM domain in SAMD9 and SAMD9L
Three-dimensional structure of SAM domain were evaluated by the University of California–San Francisco Chimera Program and PDB 2B6G of a protein data bank administered by the RCSB (Research Collaboratory for Structural Bioinformatics). Wild type (Left) and His32Leu and Leu50Ser variants (Right) were shown respectively.



Supplemental Figure 7. Cell proliferation curves for wild type (WT) or mutants of SAMD9/SAMD9L before and after doxycycline induction

Supplementary Table 1. A novel *SAMD9L* variant identified in a family with thrombocytopenia

Chr	7
Start	92763736
End	92763736
Ref	A
Alt	G
Function	exonic
Genes	*SAMD9L*
ExonicFunc	nonsynonymous SNV
Alterations	SAMD9L:NM_001303500:c.T1549C:p.W517R
gnomAD frequency ALL	0.0003
gnomAD frequency AFR	0
gnomAD frequency AMR	2.98E-05
gnomAD frequency ASJ	0
gnomAD frequency EAS	0
gnomAD frequency FIN	4.49E-05
gnomAD frequency NFE	0.0006
gnomAD frequency OTH	0
gnomAD frequency SAS	0
avsnp147	rs199714577
SIFT score	0
SIFT converted rankscore	0.912
SIFT pred	D
Polyphen2 HDIV score	1
Polyphen2 HDIV rankscore	0.899
Polyphen2 HDIV pred	D
Polyphen2 HVAR score	0.992
Polyphen2 HVAR rankscore	0.79
Polyphen2 HVAR pred	D
LRT score	0
LRT converted rankscore	0.629
LRT pred	D
MutationTaster score	1
MutationTaster converted rankscore	0.487
MutationTaster pred	D
MutationAssessor score	2.8
MutationAssessor score rankscore	0.819
MutationAssessor pred	M
FATHMM score	2.15
FATHMM converted rankscore	0.193
FATHMM pred	T
PROVEAN score	-7.18
PROVEAN converted rankscore	0.942
PROVEAN pred	D

Abbreviations; AFR, African; AMR, Latno; EUR, European (Non-Finnish); ASJ, AsjkenaziJewish; EAS, East Asian; FIN, Finnish; NFE, Non-Finnish European; OTH, Other; SAS, South Asia; FATHMM, Functional Analysis through Hidden Markov Models; PROVEAN, Protein Variation Effect Analyzer

Supplementary Table 2. Panel of 46 genes for targeted capture sequencing

APC	*ETV6*	*NPM1*	*SRSF2*
ASXL1	*EZH2*	*NRAS*	*STAG2*
BCOR	*FLT3*	*PHF6*	*STAT3*
BCORL1	*GATA2*	*PRPF8*	*SUZ12*
CALR	*IDH1*	*PTPN11*	*TET2*
CBL	*IDH2*	*RAD21*	*TP53*
CEBPA	*JAK2*	*RUNX1*	*U2AF1*
CSF1R	*JAK3*	*SAMD9*	*U2AF2*
CUX1	*KDM6A*	*SAMD9L*	*WT1*
DDX41	*KIT*	*SETBP1*	*ZRSR2*
DNMT3A	*KRAS*	*SF3B1*	
EED	*NF1*	*SMC3*	

Supplementary Table 3. Targeted regions for a panel of 46 genes

Chromosome	Probes		Gene name	# of probes
	Start	End		
chr5	112043415	112043579	*APC*	1
chr5	112090588	112090722	*APC*	1
chr5	112102023	112102107	*APC*	1
chr5	112102886	112103087	*APC*	1
chr5	112111326	112111434	*APC*	1
chr5	112116487	112116600	*APC*	1
chr5	112128143	112128226	*APC*	1
chr5	112136976	112137080	*APC*	1
chr5	112151192	112151290	*APC*	1
chr5	112154663	112155041	*APC*	2
chr5	112157593	112157688	*APC*	1
chr5	112162805	112162944	*APC*	1
chr5	112163626	112163703	*APC*	1
chr5	112164553	112164669	*APC*	1
chr5	112170648	112170862	*APC*	1
chr5	112173250	112179820	*APC*	29
chr20	30946579	30946635	*ASXL1*	1
chr20	30954187	30954269	*ASXL1*	1
chr20	30956815	30956926	*ASXL1*	1
chr20	30959967	30959969	*ASXL1*	1
chr20	31015931	31016051	*ASXL1*	1
chr20	31016128	31016225	*ASXL1*	1
chr20	31017141	31017234	*ASXL1*	1
chr20	31017704	31017856	*ASXL1*	1
chr20	31019124	31019287	*ASXL1*	1
chr20	31019386	31019482	*ASXL1*	1
chr20	31020683	31020788	*ASXL1*	1
chr20	31021087	31021720	*ASXL1*	3
chr20	31022235	31025138	*ASXL1*	13
chrX	39911365	39911653	*BCOR*	2
chrX	39913139	39913295	*BCOR*	1
chrX	39913509	39913586	*BCOR*	1
chrX	39914621	39914766	*BCOR*	1
chrX	39916408	39916574	*BCOR*	1
chrX	39921392	39921646	*BCOR*	2
chrX	39921999	39922324	*BCOR*	2
chrX	39922861	39923205	*BCOR*	2
chrX	39922861	39923103	*BCOR*	2
chrX	39923589	39923852	*BCOR*	2
chrX	39930226	39930412	*BCOR*	1
chrX	39930890	39930943	*BCOR*	1
chrX	39931602	39934433	*BCOR*	13
chrX	39935707	39935785	*BCOR*	1
chrX	39937097	39937182	*BCOR*	1
chrX	129139208	129139293	*BCORL1*	1
chrX	129146554	129146644	*BCORL1*	1
chrX	129146926	129150189	*BCORL1*	15
chrX	129154960	129155125	*BCORL1*	1

chrX	129156872	129156952	*BCORL1*	1
chrX	129158965	129159354	*BCORL1*	2
chrX	129162610	129162836	*BCORL1*	1
chrX	129171342	129171508	*BCORL1*	1
chrX	129173112	129173257	*BCORL1*	1
chrX	129184692	129184769	*BCORL1*	1
chrX	129185835	129185991	*BCORL1*	1
chrX	129189829	129190108	*BCORL1*	2
chr19	13049494	13049584	*CALR*	1
chr19	13049948	13050049	*CALR*	1
chr19	13050242	13050445	*CALR*	1
chr19	13050867	13050961	*CALR*	1
chr19	13051057	13051266	*CALR*	1
chr19	13051355	13051468	*CALR*	1
chr19	13051558	13051701	*CALR*	1
chr19	13054351	13054443	*CALR*	1
chr19	13054527	13054724	*CALR*	1
chr11	119077128	119077322	*CBL*	1
chr11	119103158	119103405	*CBL*	2
chr11	119142445	119142591	*CBL*	1
chr11	119144578	119144734	*CBL*	1
chr11	119145542	119145663	*CBL*	1
chr11	119146707	119146844	*CBL*	1
chr11	119148467	119148554	*CBL*	1
chr11	119148876	119149007	*CBL*	1
chr11	119149220	119149423	*CBL*	1
chr11	119155679	119155810	*CBL*	1
chr11	119155899	119156276	*CBL*	2
chr11	119158562	119158656	*CBL*	1
chr11	119167628	119167744	*CBL*	1
chr11	119168094	119168191	*CBL*	1
chr11	119169068	119169250	*CBL*	1
chr11	119170205	119170488	*CBL*	2
chr19	33792247	33793320	*CEBPA*	5
chr5	149433635	149433787	*CSF1R*	1
chr5	149433885	149433993	*CSF1R*	1
chr5	149434800	149434899	*CSF1R*	1
chr5	149435589	149435700	*CSF1R*	1
chr5	149435782	149435904	*CSF1R*	1
chr5	149436850	149436947	*CSF1R*	1
chr5	149437067	149437155	*CSF1R*	1
chr5	149439263	149439425	*CSF1R*	1
chr5	149440425	149440535	*CSF1R*	1
chr5	149441054	149441158	*CSF1R*	1
chr5	149441286	149441412	*CSF1R*	1
chr5	149447778	149447893	*CSF1R*	1
chr5	149449436	149449626	*CSF1R*	1
chr5	149449745	149449865	*CSF1R*	1
chr5	149450019	149450134	*CSF1R*	1
chr5	149452864	149453056	*CSF1R*	1
chr5	149456839	149456998	*CSF1R*	1
chr5	149457675	149457811	*CSF1R*	1

chr5	149459615	149459899	*CSF1R*	2
chr5	149460330	149460587	*CSF1R*	2
chr5	149465942	149465990	*CSF1R*	1
chr7	101459311	101459373	*CUX1*	1
chr7	101460920	101460949	*CUX1*	1
chr7	101559395	101559505	*CUX1*	1
chr7	101671378	101671425	*CUX1*	1
chr7	101713619	101713697	*CUX1*	1
chr7	101740644	101740781	*CUX1*	1
chr7	101747616	101747739	*CUX1*	1
chr7	101754978	101755054	*CUX1*	1
chr7	101758487	101758553	*CUX1*	1
chr7	101801840	101801888	*CUX1*	1
chr7	101813726	101813830	*CUX1*	1
chr7	101821749	101821937	*CUX1*	1
chr7	101821755	101821937	*CUX1*	1
chr7	101833093	101833151	*CUX1*	1
chr7	101837122	101837170	*CUX1*	1
chr7	101838787	101838883	*CUX1*	1
chr7	101839914	101840585	*CUX1*	3
chr7	101842082	101842147	*CUX1*	1
chr7	101843351	101843452	*CUX1*	1
chr7	101844640	101845484	*CUX1*	4
chr7	101847671	101847836	*CUX1*	1
chr7	101848394	101848450	*CUX1*	1
chr7	101870647	101870949	*CUX1*	2
chr7	101877332	101877520	*CUX1*	1
chr7	101882600	101882864	*CUX1*	2
chr7	101891692	101892319	*CUX1*	3
chr7	101916637	101916764	*CUX1*	1
chr7	101917515	101917581	*CUX1*	1
chr7	101918518	101918630	*CUX1*	1
chr7	101921220	101921336	*CUX1*	1
chr7	101923329	101923412	*CUX1*	1
chr7	101924096	101924152	*CUX1*	1
chr7	101925132	101925212	*CUX1*	1
chr7	101926004	101926068	*CUX1*	1
chr7	101926313	101926379	*CUX1*	1
chr5	176938795	176938928	*DDX41*	1
chr5	176939097	176939207	*DDX41*	1
chr5	176939323	176939394	*DDX41*	1
chr5	176939497	176939646	*DDX41*	1
chr5	176939781	176939877	*DDX41*	1
chr5	176940012	176940083	*DDX41*	1
chr5	176940354	176940485	*DDX41*	1
chr5	176940686	176940848	*DDX41*	1
chr5	176941702	176941838	*DDX41*	1
chr5	176941917	176942070	*DDX41*	1
chr5	176942187	176942259	*DDX41*	1
chr5	176942686	176942822	*DDX41*	1
chr5	176942930	176942990	*DDX41*	1
chr5	176943120	176943194	*DDX41*	1

chr5	176943289	176943448	*DDX41*	1
chr5	176943726	176943836	*DDX41*	1
chr5	176943920	176943946	*DDX41*	1
chr2	25457151	25457289	*DNMT3A*	1
chr2	25458576	25458694	*DNMT3A*	1
chr2	25459805	25459874	*DNMT3A*	1
chr2	25461999	25462084	*DNMT3A*	1
chr2	25463171	25463319	*DNMT3A*	1
chr2	25463509	25463599	*DNMT3A*	1
chr2	25464431	25464576	*DNMT3A*	1
chr2	25466767	25466851	*DNMT3A*	1
chr2	25467024	25467207	*DNMT3A*	1
chr2	25467409	25467521	*DNMT3A*	1
chr2	25468122	25468201	*DNMT3A*	1
chr2	25468889	25468933	*DNMT3A*	1
chr2	25469029	25469178	*DNMT3A*	1
chr2	25469489	25469645	*DNMT3A*	1
chr2	25469920	25470027	*DNMT3A*	1
chr2	25470460	25470618	*DNMT3A*	1
chr2	25470906	25471121	*DNMT3A*	1
chr2	25472526	25472593	*DNMT3A*	1
chr2	25475063	25475066	*DNMT3A*	1
chr2	25497810	25497956	*DNMT3A*	1
chr2	25498369	25498412	*DNMT3A*	1
chr2	25505260	25505580	*DNMT3A*	2
chr2	25505310	25505580	*DNMT3A*	2
chr2	25523008	25523112	*DNMT3A*	1
chr2	25536782	25536853	*DNMT3A*	1
chr11	85956272	85956385	*EED*	1
chr11	85961338	85961490	*EED*	1
chr11	85963190	85963282	*EED*	1
chr11	85966264	85966329	*EED*	1
chr11	85967429	85967554	*EED*	1
chr11	85968557	85968638	*EED*	1
chr11	85975214	85975305	*EED*	1
chr11	85977125	85977258	*EED*	1
chr11	85979498	85979603	*EED*	1
chr11	85988022	85988180	*EED*	1
chr11	85988960	85989033	*EED*	1
chr11	85988960	85989034	*EED*	1
chr11	85989441	85989564	*EED*	1
chr12	11803062	11803094	*ETV6*	1
chr12	11905384	11905513	*ETV6*	1
chr12	11992074	11992238	*ETV6*	1
chr12	12006361	12006495	*ETV6*	1
chr12	12022358	12022903	*ETV6*	3
chr12	12037379	12037521	*ETV6*	1
chr12	12038860	12038960	*ETV6*	1
chr12	12043875	12043977	*ETV6*	1
chr7	148504741	148504798	*EZH2*	1
chr7	148506163	148506247	*EZH2*	1
chr7	148506402	148506482	*EZH2*	1

chr7	148507425	148507506	*EZH2*	1
chr7	148508717	148508812	*EZH2*	1
chr7	148511051	148511229	*EZH2*	1
chr7	148512006	148512131	*EZH2*	1
chr7	148512598	148512638	*EZH2*	1
chr7	148513776	148513870	*EZH2*	1
chr7	148514314	148514483	*EZH2*	1
chr7	148514969	148515209	*EZH2*	2
chr7	148516688	148516779	*EZH2*	1
chr7	148523546	148523724	*EZH2*	1
chr7	148523561	148523724	*EZH2*	1
chr7	148524256	148524358	*EZH2*	1
chr7	148525832	148525972	*EZH2*	1
chr7	148526820	148526940	*EZH2*	1
chr7	148529726	148529842	*EZH2*	1
chr7	148543562	148543690	*EZH2*	1
chr7	148543589	148543690	*EZH2*	1
chr7	148544274	148544390	*EZH2*	1
chr13	28578192	28578311	*FLT3*	1
chr13	28588589	28588694	*FLT3*	1
chr13	28589294	28589393	*FLT3*	1
chr13	28589727	28589838	*FLT3*	1
chr13	28592604	28592726	*FLT3*	1
chr13	28597487	28597614	*FLT3*	1
chr13	28598998	28599080	*FLT3*	1
chr13	28601225	28601378	*FLT3*	1
chr13	28602315	28602425	*FLT3*	1
chr13	28608024	28608128	*FLT3*	1
chr13	28608219	28608351	*FLT3*	1
chr13	28608438	28608544	*FLT3*	1
chr13	28609632	28609810	*FLT3*	1
chr13	28610072	28610180	*FLT3*	1
chr13	28611322	28611425	*FLT3*	1
chr13	28622412	28622580	*FLT3*	1
chr13	28623521	28623674	*FLT3*	1
chr13	28623772	28623911	*FLT3*	1
chr13	28624232	28624359	*FLT3*	1
chr13	28626682	28626811	*FLT3*	1
chr13	28631484	28631599	*FLT3*	1
chr13	28636004	28636206	*FLT3*	1
chr13	28644628	28644749	*FLT3*	1
chr13	28674605	28674647	*FLT3*	1
chr3	128199865	128200161	*GATA2*	2
chr3	128200662	128200745	*GATA2*	1
chr3	128200662	128200787	*GATA2*	1
chr3	128202703	128202848	*GATA2*	1
chr3	128204570	128205211	*GATA2*	3
chr3	128205646	128205874	*GATA2*	1
chr2	209101806	209101893	*IDH1*	1
chr2	209103795	209103957	*IDH1*	1
chr2	209104587	209104727	*IDH1*	1
chr2	209106718	209106869	*IDH1*	1

chr2	209108151	209108328	*IDH1*	1
chr2	209110043	209110148	*IDH1*	1
chr2	209113093	209113384	*IDH1*	2
chr2	209116154	209116275	*IDH1*	1
chr15	90627501	90627585	*IDH2*	1
chr15	90628048	90628140	*IDH2*	1
chr15	90628233	90628330	*IDH2*	1
chr15	90628507	90628619	*IDH2*	1
chr15	90630344	90630495	*IDH2*	1
chr15	90630671	90630807	*IDH2*	1
chr15	90631591	90631734	*IDH2*	1
chr15	90631819	90631979	*IDH2*	1
chr15	90633711	90633876	*IDH2*	1
chr15	90634785	90634876	*IDH2*	1
chr15	90645508	90645622	*IDH2*	1
chr9	5021988	5022213	*JAK2*	1
chr9	5029783	5029906	*JAK2*	1
chr9	5044403	5044520	*JAK2*	1
chr9	5050686	5050831	*JAK2*	1
chr9	5054563	5054884	*JAK2*	2
chr9	5055669	5055788	*JAK2*	1
chr9	5064883	5065040	*JAK2*	1
chr9	5066678	5066789	*JAK2*	1
chr9	5069022	5069208	*JAK2*	1
chr9	5069925	5070052	*JAK2*	1
chr9	5072492	5072626	*JAK2*	1
chr9	5073698	5073785	*JAK2*	1
chr9	5077453	5077580	*JAK2*	1
chr9	5078306	5078444	*JAK2*	1
chr9	5080229	5080380	*JAK2*	1
chr9	5080533	5080683	*JAK2*	1
chr9	5081725	5081861	*JAK2*	1
chr9	5089674	5089863	*JAK2*	1
chr9	5090446	5090570	*JAK2*	1
chr9	5090739	5090911	*JAK2*	1
chr9	5123004	5123121	*JAK2*	1
chr9	5126333	5126446	*JAK2*	1
chr9	5126684	5126788	*JAK2*	1
chr19	17937555	17937719	*JAK3*	1
chr19	17940917	17941027	*JAK3*	1
chr19	17941312	17941429	*JAK3*	1
chr19	17942037	17942209	*JAK3*	1
chr19	17942483	17942607	*JAK3*	1
chr19	17943328	17943517	*JAK3*	1
chr19	17943599	17943738	*JAK3*	1
chr19	17945380	17945530	*JAK3*	1
chr19	17945661	17945812	*JAK3*	1
chr19	17945892	17946024	*JAK3*	1
chr19	17946733	17946860	*JAK3*	1
chr19	17947938	17948022	*JAK3*	1
chr19	17948741	17948872	*JAK3*	1
chr19	17949072	17949199	*JAK3*	1

chr19	17950286	17950472	*JAK3*	1
chr19	17951039	17951150	*JAK3*	1
chr19	17952198	17952355	*JAK3*	1
chr19	17952449	17952571	*JAK3*	1
chr19	17953125	17953419	*JAK3*	2
chr19	17953836	17953981	*JAK3*	1
chr19	17954189	17954300	*JAK3*	1
chr19	17954586	17954709	*JAK3*	1
chr19	17955043	17955226	*JAK3*	1
chrX	44732798	44732958	*KDM6A*	1
chrX	44733170	44733233	*KDM6A*	1
chrX	44820529	44820637	*KDM6A*	1
chrX	44833911	44833960	*KDM6A*	1
chrX	44870206	44870264	*KDM6A*	1
chrX	44879855	44879975	*KDM6A*	1
chrX	44894176	44894230	*KDM6A*	1
chrX	44896900	44896934	*KDM6A*	1
chrX	44910954	44911047	*KDM6A*	1
chrX	44913074	44913200	*KDM6A*	1
chrX	44918251	44918349	*KDM6A*	1
chrX	44918492	44918711	*KDM6A*	1
chrX	44919267	44919401	*KDM6A*	1
chrX	44920569	44920664	*KDM6A*	1
chrX	44921892	44921993	*KDM6A*	1
chrX	44922667	44923062	*KDM6A*	2
chrX	44928824	44929602	*KDM6A*	4
chrX	44935942	44936071	*KDM6A*	1
chrX	44937645	44937750	*KDM6A*	1
chrX	44938391	44938596	*KDM6A*	1
chrX	44941821	44941885	*KDM6A*	1
chrX	44941960	44942034	*KDM6A*	1
chrX	44942705	44942853	*KDM6A*	1
chrX	44945110	44945224	*KDM6A*	1
chrX	44948988	44949175	*KDM6A*	1
chrX	44949968	44950109	*KDM6A*	1
chrX	44966655	44966781	*KDM6A*	1
chrX	44969324	44969494	*KDM6A*	1
chrX	44970627	44970653	*KDM6A*	1
chr4	55524182	55524248	*KIT*	1
chr4	55561678	55561947	*KIT*	2
chr4	55564450	55564731	*KIT*	2
chr4	55565796	55565932	*KIT*	1
chr4	55569890	55570058	*KIT*	1
chr4	55573264	55573453	*KIT*	1
chr4	55575590	55575705	*KIT*	1
chr4	55589750	55589864	*KIT*	1
chr4	55592023	55592204	*KIT*	1
chr4	55592023	55592216	*KIT*	1
chr4	55593384	55593490	*KIT*	1
chr4	55593582	55593708	*KIT*	1
chr4	55593989	55594093	*KIT*	1
chr4	55594177	55594287	*KIT*	1

chr4	55595501	55595651	*KIT*	1
chr4	55597494	55597585	*KIT*	1
chr4	55598037	55598164	*KIT*	1
chr4	55599236	55599358	*KIT*	1
chr4	55602664	55602775	*KIT*	1
chr4	55602887	55602986	*KIT*	1
chr4	55603341	55603446	*KIT*	1
chr4	55604595	55604720	*KIT*	1
chr12	25362732	25362845	*KRAS*	1
chr12	25368378	25368494	*KRAS*	1
chr12	25378548	25378707	*KRAS*	1
chr12	25380168	25380346	*KRAS*	1
chr12	25398208	25398318	*KRAS*	1
chr17	29422328	29422387	*NF1*	1
chr17	29483001	29483144	*NF1*	1
chr17	29486028	29486111	*NF1*	1
chr17	29490204	29490394	*NF1*	1
chr17	29496909	29497015	*NF1*	1
chr17	29508440	29508507	*NF1*	1
chr17	29508728	29508803	*NF1*	1
chr17	29509526	29509683	*NF1*	1
chr17	29527440	29527613	*NF1*	1
chr17	29528055	29528177	*NF1*	1
chr17	29528429	29528503	*NF1*	1
chr17	29533258	29533389	*NF1*	1
chr17	29541469	29541603	*NF1*	1
chr17	29546023	29546136	*NF1*	1
chr17	29548868	29549005	*NF1*	1
chr17	29548868	29548947	*NF1*	1
chr17	29550462	29550585	*NF1*	1
chr17	29552113	29552268	*NF1*	1
chr17	29553453	29553702	*NF1*	2
chr17	29554236	29554309	*NF1*	1
chr17	29554541	29554624	*NF1*	1
chr17	29556043	29556483	*NF1*	2
chr17	29556853	29556992	*NF1*	1
chr17	29557278	29557400	*NF1*	1
chr17	29557860	29557943	*NF1*	1
chr17	29559091	29559207	*NF1*	1
chr17	29559718	29559899	*NF1*	1
chr17	29560020	29560231	*NF1*	1
chr17	29562629	29562790	*NF1*	1
chr17	29562936	29563039	*NF1*	1
chr17	29576002	29576137	*NF1*	1
chr17	29579956	29580018	*NF1*	1
chr17	29585362	29585520	*NF1*	1
chr17	29586050	29586147	*NF1*	1
chr17	29587387	29587533	*NF1*	1
chr17	29588729	29588875	*NF1*	1
chr17	29592247	29592357	*NF1*	1
chr17	29652838	29653270	*NF1*	2
chr17	29654517	29654857	*NF1*	2

chr17	29657314	29657516	*NF1*	1
chr17	29661856	29662049	*NF1*	1
chr17	29663351	29663491	*NF1*	1
chr17	29663653	29663932	*NF1*	2
chr17	29664386	29664600	*NF1*	1
chr17	29664837	29664898	*NF1*	1
chr17	29665043	29665157	*NF1*	1
chr17	29665722	29665823	*NF1*	1
chr17	29667523	29667663	*NF1*	1
chr17	29670027	29670153	*NF1*	1
chr17	29676138	29676269	*NF1*	1
chr17	29677201	29677336	*NF1*	1
chr17	29679275	29679432	*NF1*	1
chr17	29683478	29683600	*NF1*	1
chr17	29683978	29684108	*NF1*	1
chr17	29684287	29684387	*NF1*	1
chr17	29685498	29685640	*NF1*	1
chr17	29685987	29686033	*NF1*	1
chr17	29687505	29687721	*NF1*	1
chr17	29701031	29701170	*NF1*	1
chr5	170814953	170815010	*NPM1*	1
chr5	170817055	170817134	*NPM1*	1
chr5	170818309	170818428	*NPM1*	1
chr5	170818710	170818803	*NPM1*	1
chr5	170819714	170819820	*NPM1*	1
chr5	170819918	170819982	*NPM1*	1
chr5	170827157	170827214	*NPM1*	1
chr5	170827843	170827929	*NPM1*	1
chr5	170832306	170832407	*NPM1*	1
chr5	170833401	170833406	*NPM1*	1
chr5	170834704	170834778	*NPM1*	1
chr5	170837531	170837566	*NPM1*	1
chr1	115251159	115251275	*NRAS*	1
chr1	115252190	115252349	*NRAS*	1
chr1	115256421	115256599	*NRAS*	1
chr1	115258671	115258781	*NRAS*	1
chrX	133511648	133511785	*PHF6*	1
chrX	133512035	133512136	*PHF6*	1
chrX	133527531	133527664	*PHF6*	1
chrX	133527939	133527982	*PHF6*	1
chrX	133547518	133547687	*PHF6*	1
chrX	133547521	133547687	*PHF6*	1
chrX	133547853	133547996	*PHF6*	1
chrX	133549046	133549150	*PHF6*	1
chrX	133549046	133549249	*PHF6*	1
chrX	133551199	133551332	*PHF6*	1
chrX	133559231	133559357	*PHF6*	1
chr17	1554099	1554250	*PRPF8*	1
chr17	1554402	1554604	*PRPF8*	1
chr17	1554708	1554847	*PRPF8*	1
chr17	1554942	1555082	*PRPF8*	1
chr17	1556836	1556977	*PRPF8*	1

chr17	1557071	1557310	*PRPF8*	2
chr17	1558644	1558837	*PRPF8*	1
chr17	1559686	1559859	*PRPF8*	1
chr17	1559942	1560055	*PRPF8*	1
chr17	1561547	1561675	*PRPF8*	1
chr17	1561820	1562057	*PRPF8*	2
chr17	1562651	1562842	*PRPF8*	1
chr17	1563135	1563295	*PRPF8*	1
chr17	1563726	1563872	*PRPF8*	1
chr17	1563992	1564121	*PRPF8*	1
chr17	1564287	1564456	*PRPF8*	1
chr17	1564565	1564700	*PRPF8*	1
chr17	1564905	1565084	*PRPF8*	1
chr17	1565200	1565447	*PRPF8*	2
chr17	1576375	1576491	*PRPF8*	1
chr17	1576651	1576861	*PRPF8*	1
chr17	1577040	1577186	*PRPF8*	1
chr17	1577736	1577974	*PRPF8*	2
chr17	1578446	1578633	*PRPF8*	1
chr17	1578914	1579106	*PRPF8*	1
chr17	1579222	1579348	*PRPF8*	1
chr17	1579501	1579664	*PRPF8*	1
chr17	1579799	1580005	*PRPF8*	1
chr17	1580270	1580466	*PRPF8*	1
chr17	1580859	1580988	*PRPF8*	1
chr17	1581812	1581946	*PRPF8*	1
chr17	1582056	1582175	*PRPF8*	1
chr17	1582311	1582500	*PRPF8*	1
chr17	1582585	1582704	*PRPF8*	1
chr17	1582903	1583093	*PRPF8*	1
chr17	1584020	1584125	*PRPF8*	1
chr17	1584223	1584348	*PRPF8*	1
chr17	1584772	1584984	*PRPF8*	1
chr17	1585114	1585332	*PRPF8*	1
chr17	1585423	1585587	*PRPF8*	1
chr17	1586827	1586995	*PRPF8*	1
chr17	1587766	1587865	*PRPF8*	1
chr12	112856916	112856929	*PTPN11*	1
chr12	112884080	112884202	*PTPN11*	1
chr12	112888122	112888316	*PTPN11*	1
chr12	112890999	112891191	*PTPN11*	1
chr12	112892368	112892484	*PTPN11*	1
chr12	112893754	112893867	*PTPN11*	1
chr12	112910748	112910844	*PTPN11*	1
chr12	112915455	112915534	*PTPN11*	1
chr12	112915661	112915819	*PTPN11*	1
chr12	112919878	112920009	*PTPN11*	1
chr12	112924279	112924433	*PTPN11*	1
chr12	112924279	112924434	*PTPN11*	1
chr12	112926247	112926314	*PTPN11*	1
chr12	112926828	112926979	*PTPN11*	1
chr12	112939948	112940060	*PTPN11*	1

chr12	112942499	112942565	*PTPN11*	1
chr8	117859742	117859930	*RAD21*	1
chr8	117861185	117861268	*RAD21*	1
chr8	117862857	117863006	*RAD21*	1
chr8	117864187	117864335	*RAD21*	1
chr8	117864788	117864947	*RAD21*	1
chr8	117866484	117866707	*RAD21*	1
chr8	117868405	117868527	*RAD21*	1
chr8	117868885	117869010	*RAD21*	1
chr8	117869506	117869712	*RAD21*	1
chr8	117870591	117870697	*RAD21*	1
chr8	117874080	117874179	*RAD21*	1
chr8	117875369	117875498	*RAD21*	1
chr8	117878825	117878968	*RAD21*	1
chr21	36164435	36164907	*RUNX1*	3
chr21	36171598	36171759	*RUNX1*	1
chr21	36193968	36193993	*RUNX1*	1
chr21	36206707	36206898	*RUNX1*	1
chr21	36231771	36231875	*RUNX1*	1
chr21	36252854	36253010	*RUNX1*	1
chr21	36259140	36259409	*RUNX1*	2
chr21	36259140	36259393	*RUNX1*	2
chr21	36265222	36265260	*RUNX1*	1
chr21	36421139	36421196	*RUNX1*	1
chr7	92730644	92735410	*SAMD9*	21
chr7	92760533	92765284	*SAMD9L*	21
chr18	42281312	42281797	*SETBP1*	3
chr18	42449195	42449248	*SETBP1*	1
chr18	42456530	42456715	*SETBP1*	1
chr18	42529846	42533305	*SETBP1*	16
chr18	42618450	42618620	*SETBP1*	1
chr18	42643044	42643660	*SETBP1*	3
chr2	198257030	198257185	*SF3B1*	1
chr2	198257696	198257912	*SF3B1*	1
chr2	198260780	198261052	*SF3B1*	2
chr2	198262709	198262840	*SF3B1*	1
chr2	198263185	198263305	*SF3B1*	1
chr2	198264779	198264890	*SF3B1*	1
chr2	198264976	198265158	*SF3B1*	1
chr2	198265439	198265660	*SF3B1*	1
chr2	198266124	198266249	*SF3B1*	1
chr2	198266466	198266612	*SF3B1*	1
chr2	198266709	198266854	*SF3B1*	1
chr2	198267280	198267550	*SF3B1*	2
chr2	198267673	198267759	*SF3B1*	1
chr2	198268309	198268488	*SF3B1*	1
chr2	198269800	198269901	*SF3B1*	1
chr2	198269999	198270196	*SF3B1*	1
chr2	198272722	198272843	*SF3B1*	1
chr2	198273093	198273305	*SF3B1*	1
chr2	198274494	198274731	*SF3B1*	2
chr2	198281465	198281635	*SF3B1*	1

chr2	198283233	198283312	*SF3B1*	1
chr2	198283659	198283675	*SF3B1*	1
chr2	198285152	198285266	*SF3B1*	1
chr2	198285753	198285857	*SF3B1*	1
chr2	198288532	198288698	*SF3B1*	1
chr2	198299696	198299723	*SF3B1*	1
chr10	112327575	112327589	*SMC3*	1
chr10	112328696	112328771	*SMC3*	1
chr10	112333465	112333503	*SMC3*	1
chr10	112335094	112335161	*SMC3*	1
chr10	112337179	112337250	*SMC3*	1
chr10	112337593	112337672	*SMC3*	1
chr10	112338386	112338464	*SMC3*	1
chr10	112340662	112340779	*SMC3*	1
chr10	112341681	112341856	*SMC3*	1
chr10	112342320	112342400	*SMC3*	1
chr10	112343142	112343306	*SMC3*	1
chr10	112343599	112343720	*SMC3*	1
chr10	112343941	112344154	*SMC3*	1
chr10	112349363	112349466	*SMC3*	1
chr10	112349650	112349749	*SMC3*	1
chr10	112350170	112350330	*SMC3*	1
chr10	112350749	112350890	*SMC3*	1
chr10	112352831	112352981	*SMC3*	1
chr10	112356156	112356308	*SMC3*	1
chr10	112357897	112358048	*SMC3*	1
chr10	112359412	112359570	*SMC3*	1
chr10	112360197	112360304	*SMC3*	1
chr10	112360780	112360888	*SMC3*	1
chr10	112361395	112361642	*SMC3*	2
chr10	112361724	112361936	*SMC3*	1
chr10	112362232	112362423	*SMC3*	1
chr10	112362583	112362760	*SMC3*	1
chr10	112362942	112363048	*SMC3*	1
chr10	112363989	112364057	*SMC3*	1
chr17	74732246	74732546	*SRSF2*	2
chr17	74732881	74733242	*SRSF2*	2
chrX	123156478	123156521	*STAG2*	1
chrX	123159690	123159768	*STAG2*	1
chrX	123164811	123164975	*STAG2*	1
chrX	123171377	123171473	*STAG2*	1
chrX	123176419	123176495	*STAG2*	1
chrX	123179014	123179218	*STAG2*	1
chrX	123181204	123181355	*STAG2*	1
chrX	123182855	123182928	*STAG2*	1
chrX	123184036	123184159	*STAG2*	1
chrX	123184971	123185069	*STAG2*	1
chrX	123185165	123185244	*STAG2*	1
chrX	123189978	123190085	*STAG2*	1
chrX	123191716	123191827	*STAG2*	1
chrX	123195074	123195191	*STAG2*	1
chrX	123195621	123195724	*STAG2*	1

chrX	123196752	123196844	*STAG2*	1
chrX	123196966	123197055	*STAG2*	1
chrX	123197698	123197901	*STAG2*	1
chrX	123199726	123199796	*STAG2*	1
chrX	123200025	123200112	*STAG2*	1
chrX	123200206	123200286	*STAG2*	1
chrX	123202414	123202506	*STAG2*	1
chrX	123204999	123205173	*STAG2*	1
chrX	123210182	123210321	*STAG2*	1
chrX	123211807	123211908	*STAG2*	1
chrX	123215230	123215378	*STAG2*	1
chrX	123217271	123217399	*STAG2*	1
chrX	123220397	123220620	*STAG2*	1
chrX	123224425	123224614	*STAG2*	1
chrX	123224704	123224814	*STAG2*	1
chrX	123227868	123227994	*STAG2*	1
chrX	123229222	123229299	*STAG2*	1
chrX	123234424	123234444	*STAG2*	1
chr17	40467766	40467818	*STAT3*	1
chr17	40468807	40468919	*STAT3*	1
chr17	40468848	40468869	*STAT3*	1
chr17	40469200	40469242	*STAT3*	1
chr17	40474300	40474512	*STAT3*	1
chr17	40474303	40474512	*STAT3*	1
chr17	40475022	40475161	*STAT3*	1
chr17	40475278	40475372	*STAT3*	1
chr17	40475591	40475643	*STAT3*	1
chr17	40476729	40476864	*STAT3*	1
chr17	40476981	40477079	*STAT3*	1
chr17	40478134	40478217	*STAT3*	1
chr17	40481428	40481475	*STAT3*	1
chr17	40481572	40481665	*STAT3*	1
chr17	40481765	40481794	*STAT3*	1
chr17	40483490	40483549	*STAT3*	1
chr17	40485691	40485783	*STAT3*	1
chr17	40485909	40486067	*STAT3*	1
chr17	40489453	40489604	*STAT3*	1
chr17	40489781	40489875	*STAT3*	1
chr17	40490749	40490830	*STAT3*	1
chr17	40491332	40491427	*STAT3*	1
chr17	40497577	40497675	*STAT3*	1
chr17	40498587	40498731	*STAT3*	1
chr17	40500407	40500534	*STAT3*	1
chr17	30264266	30264539	*SUZ12*	2
chr17	30267305	30267351	*SUZ12*	1
chr17	30267441	30267505	*SUZ12*	1
chr17	30274636	30274704	*SUZ12*	1
chr17	30293166	30293215	*SUZ12*	1
chr17	30300165	30300250	*SUZ12*	1
chr17	30302501	30302732	*SUZ12*	2
chr17	30303540	30303633	*SUZ12*	1
chr17	30310018	30310123	*SUZ12*	1

chr17	30315339	30315516	*SUZ12*	1
chr17	30320261	30320352	*SUZ12*	1
chr17	30320884	30321027	*SUZ12*	1
chr17	30321583	30321740	*SUZ12*	1
chr17	30322583	30322781	*SUZ12*	1
chr17	30323817	30323896	*SUZ12*	1
chr17	30325677	30326019	*SUZ12*	2
chr4	106155100	106158594	*TET2*	16
chr4	106155100	106158508	*TET2*	15
chr4	106162496	106162586	*TET2*	1
chr4	106163991	106164084	*TET2*	1
chr4	106164727	106164935	*TET2*	1
chr4	106180776	106180926	*TET2*	1
chr4	106182916	106183005	*TET2*	1
chr4	106190767	106190904	*TET2*	1
chr4	106193721	106194075	*TET2*	2
chr4	106196205	106197673	*TET2*	7
chr17	7572930	7573008	*TP53*	1
chr17	7573927	7574033	*TP53*	1
chr17	7576540	7576584	*TP53*	1
chr17	7576628	7576657	*TP53*	1
chr17	7576853	7576926	*TP53*	1
chr17	7577019	7577155	*TP53*	1
chr17	7577499	7577608	*TP53*	1
chr17	7578177	7578289	*TP53*	1
chr17	7578371	7578554	*TP53*	1
chr17	7578371	7578533	*TP53*	1
chr17	7579312	7579569	*TP53*	2
chr17	7579312	7579590	*TP53*	2
chr17	7579700	7579721	*TP53*	1
chr17	7579839	7579912	*TP53*	1
chr21	44513215	44513359	*U2AF1*	1
chr21	44514581	44514673	*U2AF1*	1
chr21	44514765	44514898	*U2AF1*	1
chr21	44515548	44515646	*U2AF1*	1
chr21	44515804	44515833	*U2AF1*	1
chr21	44515804	44515853	*U2AF1*	1
chr21	44520563	44520629	*U2AF1*	1
chr21	44521476	44521542	*U2AF1*	1
chr21	44524425	44524512	*U2AF1*	1
chr21	44527561	44527604	*U2AF1*	1
chr19	56166471	56166519	*U2AF2*	1
chr19	56170576	56170711	*U2AF2*	1
chr19	56171543	56171587	*U2AF2*	1
chr19	56171882	56171985	*U2AF2*	1
chr19	56172404	56172555	*U2AF2*	1
chr19	56173868	56173984	*U2AF2*	1
chr19	56174972	56175110	*U2AF2*	1
chr19	56179873	56179952	*U2AF2*	1
chr19	56180036	56180158	*U2AF2*	1
chr19	56180449	56180535	*U2AF2*	1
chr19	56180449	56180547	*U2AF2*	1

chr19	56180810	56181058	*U2AF2*	2
chr19	56185300	56185431	*U2AF2*	1
chr11	32410607	32410725	*WT1*	1
chr11	32413518	32413610	*WT1*	1
chr11	32413527	32413610	*WT1*	1
chr11	32414212	32414301	*WT1*	1
chr11	32417803	32417953	*WT1*	1
chr11	32421494	32421590	*WT1*	1
chr11	32438036	32438086	*WT1*	1
chr11	32439123	32439200	*WT1*	1
chr11	32449502	32449604	*WT1*	1
chr11	32450043	32450165	*WT1*	1
chr11	32452076	32452085	*WT1*	1
chr11	32456246	32456891	*WT1*	3
chrX	15808619	15808659	*ZRSR2*	1
chrX	15809057	15809136	*ZRSR2*	1
chrX	15817995	15818076	*ZRSR2*	1
chrX	15821811	15821919	*ZRSR2*	1
chrX	15822234	15822320	*ZRSR2*	1
chrX	15826356	15826394	*ZRSR2*	1
chrX	15827323	15827441	*ZRSR2*	1
chrX	15833800	15834013	*ZRSR2*	1
chrX	15836710	15836765	*ZRSR2*	1
chrX	15838330	15838439	*ZRSR2*	1
chrX	15840854	15841362	*ZRSR2*	3

Supplementary Table 4. Rare *SAMD9/SAMD9L* germline variants in our cohort (n = 26)

UPN	Age[#]	Sex	Diagnosis[†]	Gene	Alterations	VAFs of germline[¶]	VAFs of tumor	Chr7 copy number alteration[‡]	Frequency in healthy controls*	Family history	Bone marrow cellularity	Infectious history	IgG (mg/dL)[§]
UPN004	78	F	MDS	*SAMD9L*	I327V	49%	53%	-7	.02%	-	60%	-	NA
UPN005	77	M	sAML	*SAMD9L*	L1323fs	50%	90%	-7	<.01%	-	50%	-	NA
UPN006	73	M	MDS	*SAMD9*	Q154X, I268T	46%, 47%	40%, 41%	No	.01%, <.01%	NA	50%	NA	NA
UPN007	88	F	MDS/MPN	*SAMD9*	H32L	38%	45%	No	.04%	NA	90%	NA	NA
UPN012	83	F	MDS	*SAMD9*	T205P	39%	49%	No	.08%	-	80%	NA	NA
UPN013	78	F	MDS	*SAMD9*	T205P	47%	46%	No	.08%	-	70%	NA	NA
UPN014	49	F	MDS	*SAMD9*	R221Q	54%	48%	No	.02%	-	70%	Pneumonia due to *Pseudomonas aeruginosa*	308
UPN015	66	M	MDS/MPN	*SAMD9*	I268T	44%	47%	No	<.01%	NA	60%	NA	NA
UPN017	75	M	MDS/MPN	*SAMD9*	D550V	44%	51%	No	0%	-	20%	-	NA
UPN020	79	M	MDS	*SAMD9*	N1244D	42%	48%	No	<.01%	NA	30%	NA	NA
UPN022	73	M	MDS	*SAMD9L*	L50S	48%	49%	No	0%	NA	40%	NA	NA
UPN023	86	F	MDS	*SAMD9L*	P123L	46%	52%	No	.02%	Breast cancer (M)	30%	-	NA
UPN024	61	F	MDS	*SAMD9L*	E220G	47%	46%	No	.01%	-	70%	NA	NA
UPN025	42	M	MDS	*SAMD9L*	G235S	45%	47%	No	.01%	-	40%	NA	NA
UPN026	70	F	AA/PNH	*SAMD9L*	W333C	-	45%	No	0%	-	<5%	-	NA
UPN028	34	F	AA/PNH	*SAMD9L*	A637T	-	53%	No	.02%	-	30%	-	985
UPN029	59	M	MDS	*SAMD9L*	S728P, Y705C	48%, 51%	55%, 47%	No	.02%, .01%	NA	50%	NA	NA
UPN_ADD1	61	F	MDS	*SAMD9*	A949S	-	36%	No	.08%	-	60%	-	1490
UPN_ADD2	75	F	MDS	*SAMD9*	R106H	-	53%	No	.02%	-	90%	-	NA
UPN_ADD3	41	F	MDS	*SAMD9*	R902Q	-	49%	No	<.01%	-	10%	Positive blood culture including *VRE, Klebsiella* , and *C. albicans*	352
UPN_ADD4	78	F	MDS	*SAMD9L*	R1298G	-	54%	No	<.01%	-	60%	-	544
UPN_ADD5	52	M	AA/PNH	*SAMD9L*	A637S	-	45%	No	<.01%	-	20%	-	NA
UPN_ADD6	57	M	MDS	*SAMD9L*	G247A	-	48%	No	0%	-	50%	Pneumonia due to *Pneumocystis jirovecii*	1,120
UPN_ADD7	70	M	sAML	*SAMD9*	T1370fs	-	51%	No	.02%	-	40%	-	590

[#]Median age and range; 72 (34-88) in patients with *SAMD9/SAMD9L* variants (n = 24) *vs.* 68 (17-94) in patients without them (n = 775), *P* = 0.3 (T test)

[†]Previous treatment history; 0% (0/24) in patients with SAMD9/SAMD9L variants *vs.* 0.6% (5/775) in patients without them, *P* = 1 (Fisher's exact test)

[¶] "-" depicts that germline DNAs were not available.

[‡]Aberrant karyotype; 46% (11/24) in patients with *SAMD9/SAMD9L* variants *vs.* 28% (220/775) in patients without them, *P* = 0.07 (Fisher's exact test); Cytogenetic subsets in detal were shown (Supplemental table 7)

*Ethnically-matched healthy controls from gnomAD (n = 99,860) (Supplemental Figure 1)

[§]Immunoglobulin G; normal range; 717-1,411 (mg/dl)

Abbreviations; UPN, universal patient number; sAML, secondary acute myeloid leukemia; MDS, myelodysplastic syndrome; -7, monosomy 7; VAFs, variant allele frequencies; NA, not applicable; M, mother; VRE, vancomycin resistant Enterococci; C. albicans, Candida albicans.

Supplementary Table 5. Truly pathogenic SAMD9 germ line variants (n=23)

Amino Acid change	Prediction (3≥positive)
SAMD9:A1195V	Pathogenic
SAMD9:I983S	Pathogenic
SAMD9:R982H	Pathogenic
SAMD9:R982C	Pathogenic
SAMD9:I897M	Pathogenic
SAMD9:Y684C	Pathogenic
SAMD9:L641P	Pathogenic
SAMD9:R1293Q	VUS
SAMD9:R1293W	VUS
SAMD9:Q1286K	VUS
SAMD9:P1280L	VUS
SAMD9:E1136Q	VUS
SAMD9:F1017V	VUS
SAMD9:E974K	VUS
SAMD9:R824Q	VUS
SAMD9:K821M	VUS
SAMD9:D769N	VUS
SAMD9:D769G	VUS
SAMD9:A722E	VUS
SAMD9:R685Q	VUS
SAMD9:K1569N	VUS
SAMD9:L1539I	VUS
SAMD9:R459Q	VUS

Abbreviations; P, pathogenic; VUS, variants of unknown significance

Supplementary Table 6. Area Under the Curve (AUC) for 8 prediction algorithms

Algorithms	AUC
PolyPhen-2	0.823
Mutation Assessor	0.810
MutationTaster	0.780
SIFT	0.777
PROVEAN	0.764
M-CAP	0.726
DANN	0.712
CADD	0.688

Supplementary Table 7. *SAMD9* and S*AMD9L* missense rare variants with predicted pathogenesis based on top 5 algorithms

UPN	Gene	Alterations	Predicted pathogenesis
UPN006	*SAMD9*	I268T	P
UPN012	*SAMD9*	T205P	P
UPN013	*SAMD9*	T205P	P
UPN015	*SAMD9*	I268T	P
UPN017	*SAMD9*	D550V	P
UPN022	*SAMD9L*	L50S	P
UPN024	*SAMD9L*	E220G	P
UPN025	*SAMD9L*	G235S	P
UPN026	*SAMD9L*	W333C	P
UPN_ADD6	*SAMD9L*	G247A	P
UPN029	*SAMD9L*	S728P, Y705C	VUS, P
UPN007	*SAMD9*	H32L	VUS
UPN014	*SAMD9*	R221Q	VUS
UPN020	*SAMD9*	N1244D	VUS
UPN_ADD1	*SAMD9*	A949S	VUS
UPN_ADD2	*SAMD9*	R106H	VUS
UPN_ADD3	*SAMD9*	R902Q	VUS
UPN004	*SAMD9L*	I327V	VUS
UPN023	*SAMD9L*	P123L	VUS
UPN028	*SAMD9L*	A637T	VUS
UPN_ADD4	*SAMD9L*	R1298G	VUS
UPN_ADD5	*SAMD9L*	A637S	VUS

Abbreviations; P, pathogenic; VUS, variants of unknown significance

Supplementary Table 8. Rare SAMD9/SAMD9L GL variants in myeloid neoplasms database (n = 7)

Sample	Age	Sex	Genes	Alterations	Location	Diagnosis	Subtypes	Frequency in healthy controls	Predicted pathogenesis
UPN39	88	F	*SAMD9*	H32L	N-terminus	MDS/MPN	CMML	0.04%	VUS
AML139	58	M	*SAMD9*	I247T	N-terminus	AML	Normal Karyotype, *NPM1* mutations	<.01%	P
UPN41	66	M	*SAMD9*	I268T	N-terminus	MDS/MPN	CMML	<.01%	P
PD9412	NA	NA	*SAMD9*	L574P	Central	MPN	PMF	<.01%	P
AML082	37	M	*SAMD9*	Q1427P	C-terminus	AML	46, XY, del (11) (q14 q25), *CEBPA* (double mutant)	0%	VUS
PD4780	NA	NA	*SAMD9L*	C228Y	N-terminus	MPN	PMF	<.01%	P
PD4996	NA	NA	*SAMD9L*	R285Q	N-terminus	MPN	PMF	<.01%	VUS

Abbreviations; NA, not applicable; CMML, Chronic myelomonocytic leukemia; PMF, primary myelofibrosis; P, pathogenic; VUS, variants of ur

Supplementary Table 9. Three gene locations of *SAMD9* and *SAMD9L*

Gene	Locations	Amino acids
SAMD9	N-terminal	1-530
SAMD9	Center	531-1,060
SAMD9	C-terminal	1,061-1,589
SAMD9L	N-terminal	1-528
SAMD9L	Center	529-1,056
SAMD9L	C-terminal	1,057-1,584

Supplementary Table 10. Cytogenetics of adult MDS patients with *SAMD9*/*SAMD9L* variants and -7

UPN	Cytogenetics	Gene	Alterations	VAFs of germline	VAFs of tumor
UPN004	44,XX,-4,del(5)(q12q33),-17,add(19)(p13)[3]/45,sl,-add(19)(p13),+19,+mar1[7]/44,sl1,-6,+inv(6)(p23q25),**-7**,-10,+del(10)(q25),-14,+add(14)(q32),-15,-22,+der(22)t(15;22)(q11.2;q13),+mar2[cp6]/46,XX[4]	*SAMD9L*	I327V	49%	53%
UPN005	42,XY,add(1)(q32),del(3)(q12),add(4)(q21),del(5)(q22q35),**-7**,der(12)t(12;13)(p13;q12),-13,-13,-16,-18,+mar1[cp20]	*SAMD9L*	L1323fs	50%	90%
UPN006	46,XY[20]	*SAMD9*	Q154X, I268T	46%, 47%	40%, 41%
UPN007	46,XX[20]	*SAMD9*	H32L	38%	45%
UPN012	46,XX,del(5)(q13q33)[14]/46,XX[6]	*SAMD9*	T205P	39%	49%
UPN013	46,XX,del(5)(q13q33)[6]/46,XX[14]	*SAMD9*	T205P	47%	46%
UPN014	47, XX, +21[20]	*SAMD9*	R221Q	54%	48%
UPN015	46,XY[20]	*SAMD9*	I268T	44%	47%
UPN017	46,XY[cp30]	*SAMD9*	D550V	44%	51%
UPN020	46, XY[20]	*SAMD9*	N1244D	42%	48%
UPN022	45, X, -Y[20]	*SAMD9L*	L50S	48%	49%
UPN023	46,XX[20]	*SAMD9L*	P123L	46%	52%
UPN024	46,XY,del(5)(q13q33)[1]/46,XX[4]	*SAMD9L*	E220G	47%	46%
UPN025	46,XY,del(5)(q13q33),-18,del(20)(q11.2q13.1)[4]/46,XY[16]	*SAMD9L*	G235S	45%	47%
UPN026	46,XX[20]	*SAMD9L*	W333C	-	45%
UPN028	46,XX[20]	*SAMD9L*	A637T	-	53%
UPN029	46,XY[20]	*SAMD9L*	S728P, Y705C	48%, 51%	55%, 47%
UPN_ADD1	46,XX[20]	*SAMD9*	A949S	-	36%
UPN_ADD2	44-46,XX, del(5)(q21q23),add(7)(q11.2), add(12)(p13), +1-2 mar(CP)[20]	*SAMD9*	R106H	-	53%
UPN_ADD3	46,XY[20]	*SAMD9*	R902Q	-	49%
UPN_ADD4	46,XX,del(20)(q11.2q13.1)[5]/46,XX[15]	*SAMD9L*	R1298G	-	54%
UPN_ADD5	46,XY[20]	*SAMD9L*	A637S	-	45%
UPN_ADD6	42-44,XY,der(5)del(5)(q13.3)t(5;12)(q13.3;q13), der(12)t(5;12),-15,-16, -17,-18, der(19)t(17;19)(q21;p13.3),add(20)(q13.3),add(21)(q22)[cp20]	*SAMD9L*	G247A	-	48%
UPN_ADD7	46,XY[20]	*SAMD9*	T1370fs	-	51%

"-" depicts germline DNAs were not available. Abbreviations; VAFs, variant allele frequencies

Supplemental Table 11. Summary of cell proliferation assay (n=13)

Gene	Mutants	Prediction	Deteced cohort	Results of cell proliferation assay
SAMD9	T205P	Pathogenic missense	Our MDS cohort	LOF
SAMD9	I247T	Pathogenic missense	Public database	LOF
SAMD9	I268T	Pathogenic missense	Our MDS cohort and public database	WT
SAMD9	D550V	Pathogenic missense	Our MDS cohort	WT
SAMD9	L574P	Pathogenic missense	Public database	LOF
SAMD9L	L50S	Pathogenic missense	Our MDS cohort	WT
SAMD9L	C228Y	Pathogenic missense	Public database	LOF
SAMD9L	E220G	Pathogenic missense	Our MDS cohort	LOF
SAMD9L	G235S	Pathogenic missense	Our MDS cohort	LOF
SAMD9L	G247A	Pathogenic missense	Our MDS cohort	WT
SAMD9L	W333C	Pathogenic missense	Our MDS cohort	LOF
SAMD9L	W517R	Pathogenic missense	Index familal cases	LOF
SAMD9L	L1323fs	Frameshift	Our MDS cohort	LOF

Supplemental Table 12. Comparison of pathogenic features of GL SAMD9/SAMD9L variants

Parameters	Pediatric MDS	Adult MDS
Distribution of genetic variants	C-terminus	N-terminus
Genetic reversion	Frequent	Rare
Latency	Short	Long
Function of GL alterations	Gain-of-function	Loss-of-function