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Supplemental Methods

NGS for CH determination

Peripheral blood samples from participants were collected in PAXgene tubes (Qiagen), stored at -20°C before use, and DNA was isolated according to the standard kit protocols. Thereafter, amplicon library generation and next-generation sequencing (NGS) were performed as previously described and applied to a myelodysplastic syndrome clinical trial.[1] Briefly, 15-20 ng of bead-purified DNA (AxyPrep FragmentSelect-I beads, Axygen MAG-FRAG-I-5) was converted into barcoded DNA libraries using the Ion Torrent next-generation sequencing kit (Thermo Fisher Scientific), and purified again (AMPure XP beads, Beckman Coulter A63881). Libraries consisted of 1554 amplicons covering a panel of 48 genes commonly mutated in myeloid cancer (see Supplemental Table 1 for the complete gene list; specific amplicon sequences available upon request). Of note, this list did not include *PPM1D*. DNA libraries were sequenced on the Ion Proton (Thermo Fisher Scientific) at Queen's Genomics Lab at Ongwanada (Kingston, ON, Canada) at a mean depth of 1757.1X (uniformity of 90.3% and 97.1% on target), aligned to the

human genome reference hg19 with tmap, and variants were annotated with Ion Reporter software (versions 4.6 – 5.6).

Variants (SNVs and indels) were filtered in based on the following inclusion rules: exonic location, non-synonymous substitution, p-value <0.01, coverage >50, VAF between 0.02 and 0.43. Furthermore, variants were excluded if: present in UCSC Common SNP Database, minor allele frequency (MAF) >0.02, Global/European/American MAF >0.02. This filtered list was visually inspected in the Integrative Genomics Viewer (IGV, Broad Institute) to rule out false positives (on amplicon edges, strand bias, poor mapping quality, and presence in other samples). Borderline filtered out variants were evaluated as well. Next, variants were excluded if they did not meet previously vetted criteria for candidate driver mutations.[2] Finally, a sampling of CH variant calls were confirmed (20/21) using an independent NGS platform (HiSeq 4000, Illumina; data not shown) as part of a separate RNA-seq study (in prep.).

Laboratory blood values

A clinical laboratory at Sunnybrook Hospital (Toronto, Canada) quantified blood values: hemoglobin, platelets, monocytes, white blood cells (WBC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), red blood cell distribution width (RDW), mean corpuscular volume (MCV), reticulocyte count, lactate dehydrogenase (LDH), ferritin, iron, total iron binding capacity (TIBC), vitamin B12, thyroid stimulating hormone (TSH), C-reactive protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin (t bili), creatinine, creatinine clearance, albumin, calcium.

Cytokines

Blood samples were allowed to clot for 15-20 min and then centrifuged for 12 min at 2000 x g and 4°C, cryopreserved serum was aliquoted and a subset (N=297) run on a 42-plex cytokine array (SKU HD42, Eve Technologies, Calgary, AB, Canada) to quantify cytokine/chemokine levels (EGF, FGF-2, Eotaxin-1, TGFα, G-CSF, Flt-3L, GM-CSF, Fractalkine, IFNa2, IFNy, GROa, IL-10, MCP-3, IL-12 P40, MDC, IL-12 P70, PDGF-AA, IL-13, PDGF-BB, IL-15, sCD40L, IL-17A, IL-1RA, IL-

1α, IL-9, IL-1ß, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IP-10/CXCL-10, MCP-1, MIP-1α, MIP-1ß, RANTES, TNFα, TNFß, VEGFA, IL-18).

Statistics

The study was originally designed to determine the prevalence of CH (unknown in early 2014) and the proportion of CH with lab abnormalities (particularly anemia) and comorbidities. We determined our sample size according to an OR we felt was clinically significant (OR=4). We assumed: 1. 20-30% anemic participants would comprise cases and 70-80% non-anemic participants controls; 2. 33% of anemia would be unexplainable (defined as not potentially attributable to iron or vitamin B12 deficiency, renal insufficiency (creatinine clearance <30ml/min) or inflammatory states (CRP >10mg/L)) and 33% of these would harbour CH. The expected exposure rate of CH was therefore 10.9% (0.33×0.33) among cases. We calculated a sample size up to 420 was expected to be required to achieve 80% power and 5% significance level (2-sided).

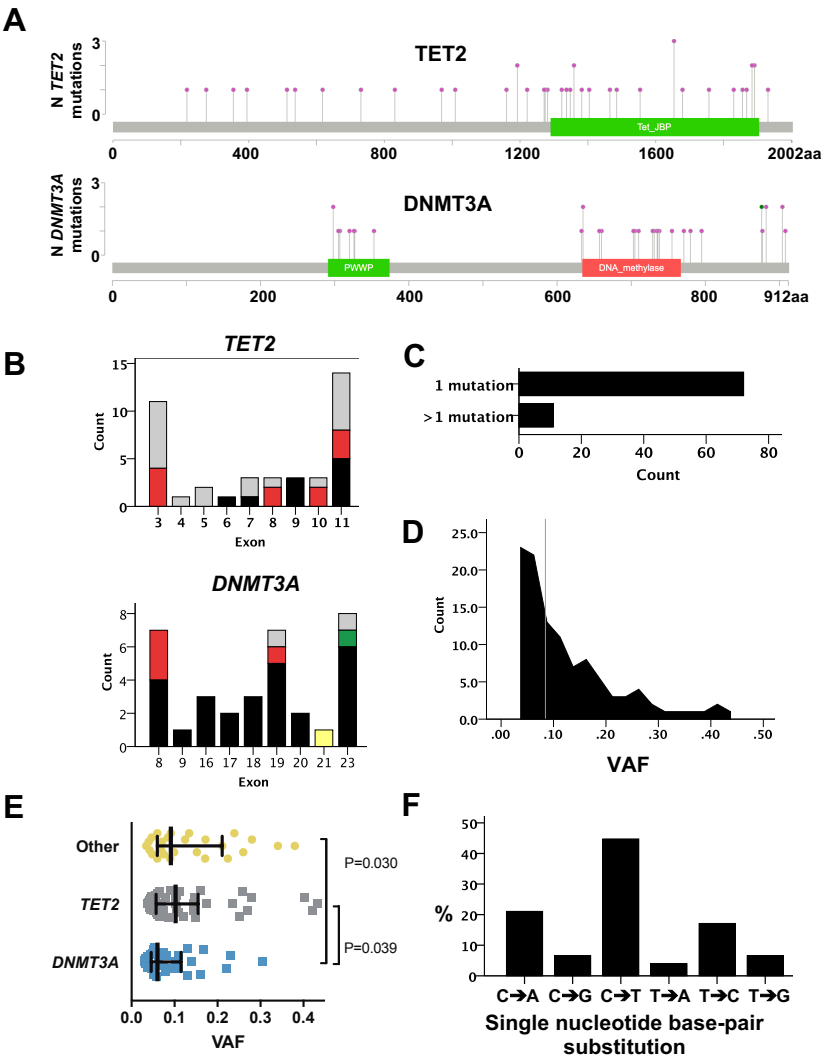
The following categorical groups were compared in post-hoc analyses: any mutation (CH) vs. no mutation, VAF>0.1 ($CH_{VAF>0.1}$) vs. VAF≤0.1 or no mutation call, >1 mutation ($CH_{mut>1}$) vs. 1 or no mutation, *TET2* mutation (CH_{TET2}) vs. no mutation, and *DNMT3A* mutation (CH_{DNMT3A}) vs. no mutation. For plotted median cytokine levels, the VAF and mutation count groups were stratified further to show dose-response.

References

1. Sekeres MA, Othus M, List AF, et al. Randomized Phase II Study of Azacitidine Alone or in Combination With Lenalidomide or With Vorinostat in Higher-Risk Myelodysplastic Syndromes and Chronic Myelomonocytic Leukemia: North American Intergroup Study SWOG S1117. *J Clin Oncol*. 2017;35(24):2745-2753.
2. Lindsley RC, Saber W, Mar BG, et al. Prognostic Mutations in Myelodysplastic Syndrome after Stem-Cell Transplantation. *N Engl J Med*. 2017;376(6):536-547.

Supplemental Figure 1. Characteristics of CH variants. (A) The location of CH mutations with respect to affected amino acids in TET2 and DNMT3A are shown on the x-axis, while the y-axis depicts the number of mutations called in the cohort. (B) Exons affected by mutations and their counts in *TET2* and *DNMT3A* (gray = frameshift; yellow = splice site; green = non-frameshift indel; red = nonsense; black = missense). (C) Number of participants with 1 mutation or >1 mutation calls. (D) Range of variant allele fraction (VAF, 0.03-0.43) by count. (E) VAF plots for CH with mutations in *DNMT3A* (yellow), *TET2* (grey) or other genes (blue) including median and interquartile range. (F) Percentage of indicated single nucleotide base-pair substitutions in CH mutation calls.

Supplemental Figure 1



Supplemental Table 1. List of genes and regions covered by custom Ion Torrent amplicon-based library panel

Name	Chromosome	Chr_Start	Chr_End	Num_Amplicons	Total_Bases	Covered_Bases	Missed_Bases	Overall_Coverage	Exons
ASXL1	chr20	31021087	31021720	7	633	633	0	1	11
ASXL1	chr20	31022235	31027122	44	4887	4653	234	0.9521	
BCOR	chrX	.	.	58	5661	5419	242	0.9573	CDS
BCORL1	chrX	.	.	57	5256	5189	67	0.9873	CDS
BOD1L	chr4	.	.	106	9416	9031	385	0.9591	CDS
BRAF	chr7	140453075	140453193	2	118	118	0	1	15
BRCC3	chrX	154299800	154299925	2	125	125	0	1	1, 4
BRCC3	chrX	154305445	154305564	2	119	119	0	1	
CALR	chr19	13054527	13055304	7	777	672	105	0.865	9
CBL	chr11	.	.	37	2881	2794	87	0.9698	CDS
CEBPA	chr19	.	.	8	1087	799	288	0.7351	CDS
CSF3R	chr1	.	.	36	3555	3444	111	0.9688	CDS
CUX1	chr7	.	.	72	5896	5361	535	0.9093	CDS
DNMT3A	chr2	.	.	45	3385	3211	174	0.9486	CDS
ETV6	chr12	.	.	18	1439	1328	111	0.9229	CDS
EZH2	chr7	.	.	36	2732	2732	0	1	CDS
FLT3	chr13	.	.	49	3222	3167	55	0.9829	CDS
GATA1	chrX	48649498	48649736	2	238	193	45	0.811	2, 3
GATA1	chrX	48650251	48650628	4	377	315	62	0.836	
GATA2	chr3	.	.	15	1587	1479	108	0.9319	CDS
GNAS	chr20	.	.	45	6100	5371	729	0.8805	CDS
GNB1	chr1	.	.	15	1113	1113	0	1	CDS
IDH1	chr2	.	.	20	1325	1236	89	0.9328	CDS
IDH2	chr15	.	.	20	1469	1334	135	0.9081	CDS
JAK2	chr9	.	.	52	3629	3596	33	0.9909	CDS
KDM6A	chrX	.	.	62	4496	4327	169	0.9624	CDS
KIT	chr4	55593384	55593490	1	106	106	0	1	8, 10, 11, 17
KIT	chr4	55593582	55593708	2	126	126	0	1	
KIT	chr4	55599236	55599358	1	122	122	0	1	
KIT	chr4	55589750	55589864	1	114	114	0	1	
KRAS	chr12	.	.	10	737	597	140	0.81	CDS
MPL	chr1	43814934	43815030	1	96	96	0	1	10
NF-E2	chr12	54688919	54689088	2	169	169	0	1	2, 3
NF-E2	chr12	54685891	54687165	12	1274	1269	5	0.9961	
NF1	chr17	.	.	132	9251	9150	101	0.9891	CDS
NPM1	chr5	.	.	17	1014	884	130	0.8718	CDS
NRAS	chr1	.	.	9	610	610	0	1	CDS
PHF6	chrX	.	.	18	1585	1585	0	1	CDS
PTPN11	chr12	112926828	112926979	2	151	151	0	1	3, 7, 8, 13
PTPN11	chr12	112888122	112888316	2	194	194	0	1	
PTPN11	chr12	112910748	112910844	2	96	96	0	1	
PTPN11	chr12	112915455	112915534	1	79	79	0	1	
RAD21	chr8	.	.	31	2026	1953	73	0.964	CDS
RIT1	chr1	.	.	11	710	710	0	1	CDS
RUNX1	chr21	.	.	20	1842	1731	111	0.9397	CDS
SETBP1	chr18	.	.	49	5040	4781	259	0.9486	CDS
SF3B1	chr2	.	.	63	4195	4154	41	0.9902	CDS
SH2B3	chr12	111855923	111856681	6	758	510	248	0.673	2
SMC1A	chrX	.	.	55	3952	3952	0	1	CDS
SMC3	chr10	.	.	60	3944	3813	131	0.9668	CDS
SRSF2	chr17	.	.	6	686	664	22	0.968	CDS
STAG2	chrX	.	.	68	4137	4072	65	0.9843	CDS
TET2	chr4	.	.	62	9607	9489	118	0.9877	CDS
TLR2	chr4	.	.	23	2365	2172	193	0.9184	CDS
TP53	chr17	.	.	22	1556	1556	0	1	CDS
U2AF1	chr21	.	.	16	920	920	0	1	CDS
WT1	chr11	32417803	32417953	2	150	150	0	1	7, 9
WT1	chr11	32413527	32413610	1	83	83	0	1	
ZRSR2	chrX	.	.	23	1559	1543	16	0.9897	CDS

Supplemental Table 2. CH/subtypes vs. age and sex						
CHIP/ARCH group comparison, N	**Possible confounding factor**	**Raw p-value**	**OR**	**Lower 95% CI**	**Upper 95% CI**	**Analyses adjusted?**
Any mutation (CH) N=83 vs. no mutation N=276						
	Age (years)	0.0123	1.04	1.009	1.072	Yes
	Sex (Male vs. Female)	0.3803	1.114	0.662	1.851	No
VAF>0.1 N=36 vs. VAF<0.1 or no mutation N=323						
	Age (years)	0.0266	1.05	1.006	1.098	Yes
	Sex (Male vs. Female)	0.538	1.249	0.603	2.514	No
Mutation count >1 N=11 vs. mutation count ≤1 N=348						
	Age (years)	0.0325	1.091	1.011	1.187	Yes
	Sex (Male vs. Female)	0.1615	2.369	0.7	8.374	No
***TET2* mutation N=34 vs. no mutation N=276**						
	Age (years)	0.0604	1.044	0.999	1.093	No
	Sex (Male vs. Female)	0.0628	1.963	0.963	4.005	No
***DNMT3A* mutation N=32 vs. no mutation N=276**						
	Age (years)	0.3442	1.022	0.978	1.069	No
	Sex (Male vs. Female)	0.3598	0.681	0.284	1.491	No

Supplemental Table 3. Complete variant call list

gene	VAF	locus	type	ref	genotype	pvalue	coverage	codon	exon	protein	coding	sift	location	function
ASXL1	0.04	chr20:310222	SNV	C	C/A	0.003355985	1302	TAA	12	p.Tyr591Ter	c.1773C>A		exonic	nonse
ASXL1	0.07	chr20:310222	SNV	C	C/A	0	2000	TAA	12	p.Tyr591Ter	c.1773C>A		exonic	nonse
BCOR	0.13	chrX:3991357	INDEL	GA	GA/G	0	828	CCC	13	p.Leu1586fs	c.4757_4757delT		exonic	frame
CBL	0.05	chr11:119149	SNV	T	T/G	2.03119E-09	1999	TGC	9	p.Phe418Cys	c.1253T>G		exonic	misse
CUX1	0.17	chr7:1018448	INDEL	TC	TC/T	0	345	CCA	18	p.Ala761fs	c.2280_2280delC		exonic	frame
DNMT3A	0.079	chr2:2545715	INDEL	CAAAAT	CAAAAT/CAA	0	1958	TTT	23	p.Tyr908fs	c.2723delA		exonic	frame
DNMT3A	0.03	chr2:2545717	SNV	G	G/A	0.015498869	1286	CTG	23	p.Pro904Leu	c.2711C>T	0	exonic	misse
DNMT3A	0.06	chr2:2545717	SNV	G	G/A	1.06812E-10	1192	CTG	23	p.Pro904Leu	c.2711C>T	0	exonic	misse
DNMT3A	0.17	chr2:2545724	SNV	G	G/A	0	2000	TGC	23	p.Arg882Cys	c.2644C>T	0	exonic	misse
DNMT3A	0.10	chr2:2545724	SNV	G	G/A	0	1999	TGC	23	p.Arg882Cys	c.2644C>T	0	exonic	misse
DNMT3A	0.051	chr2:2545725	SNV	C	C/A	1.8433E-11	1999	TTC	23	p.Val877Phe	c.2629G>T	0	exonic	misse
DNMT3A	0.052	chr2:2545725	INDEL	GTCAGTATAG	GTCAGTATAG	1.333E-12	1982		23	p.Phe870_Asp	c.2610_2627delCCCAGTCCA		exonic	nonfr
DNMT3A	0.036	chr2:2545726	SNV	T	T/G	0.000965028	2000	GCC	23	p.Asp876Ala	c.2627A>C		exonic	misse
DNMT3A	0.22	chr2:2545980	SNV	A	A/C	0	2000		21				splicesite	none
DNMT3A	0.07	chr2:2546202	SNV	C	C/A	0	1999	TTG	20	p.Trp795Leu	c.2384G>T	0	exonic	misse
DNMT3A	0.14	chr2:2546206	SNV	A	A/G	0	2000	ACT	20	p.Ile780Thr	c.2339T>C		exonic	misse
DNMT3A	0.06	chr2:2546318	SNV	G	G/A	0	1827	TGA	19	p.Arg771Ter	c.2311C>T		exonic	nonse
DNMT3A	0.05	chr2:2546322	SNV	A	A/G	3.065E-07	1781	TCT	19	p.Phe755Ser	c.2264T>C	0	exonic	misse
DNMT3A	0.13	chr2:2546326	INDEL	GGGCCGCGCA	GGGCCGCGCA	0	1691	CCA	19	p.Leu738fs	c.2213_2228delTGCATGATG		exonic	frame
DNMT3A	0.03	chr2:2546328	SNV	C	C/T	0.062324672	2000	CAC	19	p.Arg736His	c.2207G>A		exonic	misse
DNMT3A	0.05	chr2:2546328	SNV	T	T/C	5.39324E-06	1265	TGC	19	p.Tyr735Cys	c.2204A>G	0	exonic	misse
DNMT3A	0.09	chr2:2546330	SNV	A	A/T	0	917	TAC	19	p.Phe731Tyr	c.2192T>A	0	exonic	misse
DNMT3A	0.16	chr2:2546330	SNV	C	C/A	0	2000	CTG	19	p.Arg729Leu	c.2186G>T		exonic	misse
DNMT3A	0.05	chr2:2546355	SNV	A	A/T	2.11E-13	1997	AGC	18	p.Cys710Ser	c.2128T>A	0	exonic	misse
DNMT3A	0.08	chr2:2546356	SNV	A	A/G	0	2000	ACT	18	p.Ile705Thr	c.2114T>C		exonic	misse
DNMT3A	0.08	chr2:2546357	SNV	G	G/C	7.89E-13	720	GTG	18	p.Leu703Val	c.2107C>G	0	exonic	misse
DNMT3A	0.11	chr2:2546453	SNV	T	T/G	0	1998	TCC	17	p.Tyr660Ser	c.1979A>C	0.01	exonic	misse
DNMT3A	0.11	chr2:2546454	SNV	C	C/T	0	2000	ATG	17	p.Val657Met	c.1969G>A	0	exonic	misse
DNMT3A	0.05	chr2:2546680	SNV	G	G/A	1.12502E-09	2000	TGG	16	p.Arg635Trp	c.1903C>T	0	exonic	misse
DNMT3A	0.03	chr2:2546680	SNV	G	G/A	0.006777507	1999	TGG	16	p.Arg635Trp	c.1903C>T	0	exonic	misse
DNMT3A	0.038	chr2:2546680	SNV	G	G/A	0.00892627	848	CTC	16	p.Pro633Leu	c.1898C>T	0	exonic	misse
DNMT3A	0.03	chr2:2546998	SNV	G	G/C	0.00937303	2000	GGG	9	p.Ala353Gly	c.1058C>G	0.36	exonic	misse
DNMT3A	0.05	chr2:2547049	SNV	C	C/T	1.43136E-05	904	TGA	8	p.Trp327Ter	c.981G>A		exonic	nonse
DNMT3A	0.23	chr2:2547049	SNV	G	G/A	0	1996	TGC	8	p.Arg326Cys	c.976C>T	0	exonic	misse
DNMT3A	0.31	chr2:2547051	SNV	G	G/A	0	2000	TGA	8	p.Arg320Ter	c.958C>T		exonic	nonse
DNMT3A	0.13	chr2:2547055	SNV	G	G/A	0	1998	CTA	8	p.Pro307Leu	c.920C>T	0	exonic	misse
DNMT3A	0.05	chr2:2547055	SNV	C	C/T	5.04127E-10	1972	TGA	8	p.Trp305Ter	c.915G>A		exonic	nonse
DNMT3A	0.05	chr2:2547058	SNV	C	C/T	4.94857E-10	2000	GAG	8	p.Gly298Glu	c.893G>A	0	exonic	misse
DNMT3A	0.04	chr2:2547058	SNV	C	C/T	0.000238111	1997	AGG	8	p.Gly298Arg	c.892G>A	0	exonic	misse
GNAS	0.07	chr20:574844	SNV	C	C/T	0	2000	TGT	8	p.Arg844Cys	c.2530C>T	0	exonic	misse
GNAS	0.07	chr20:574844	SNV	G	G/A	1.25271E-10	663	CAT	8	p.Arg844His	c.2531G>A	0	exonic	misse
GNAS	0.09	chr20:574844	SNV	G	G/A	0	2000	CAT	8	p.Arg844His	c.2531G>A	0	exonic	misse
GNB1	0.12	chr1:1747227	SNV	C	C/A	0	1997	AAT	5	p.Lys57Asn	c.171G>T		exonic	misse
GNB1	0.172	chr1:1747229	SNV	T	T/C	0	1995	GAG	5	p.Lys57Glu	c.169A>G	0	exonic	misse
GNB1	0.152	chr1:1747229	SNV	T	T/C	0	1974	GAG	5	p.Lys57Glu	c.169A>G	0	exonic	misse
JAK2	0.10	chr9:5073770	SNV	G	G/T	0	657	TTC	14	p.Val617Phe	c.1849G>T		exonic	misse
JAK2	0.239	chr9:5073770	SNV	G	G/T	0	1990	TTC	14	p.Val617Phe	c.1849G>T	0	exonic	misse
KDM6A	0.09	chrX:4492276	SNV	C	C/T	0	1991	TAG	16	p.Gln544Ter	c.1630C>Tc.1630C>T		exonic	nonse
MPL	0.28	chr1:4381500	SNV	G	G/T	0	1995	TTG	10	p.Trp515Leu	c.1544G>T	0.25	exonic	misse
PHF6	0.06	chrX:1335276	SNV	T	T/A	5.14375E-10	932	AAC	4	p.Tyr124Asn	c.370T>A	0	exonic	misse
SF3B1	0.26	chr2:1982668	SNV	T	T/C	0	1971	GAA	15	p.Lys700Glu	c.2098A>G	0	exonic	misse
SF3B1	0.22	chr2:1982668	SNV	T	T/C	0	1981	GAA	15	p.Lys700Glu	c.2098A>G	0	exonic	misse
SF3B1	0.03	chr2:1982673	SNV	C	C/G	0.016647921	1292	AAC	14	p.Lys666Asn	c.1998G>C	0	exonic	misse

SF3B1	0.05	chr2:1982673	SNV	C	C/A	8.04915E-09	1998	AAT	14	p.Lys666Asn	c.1998G>T		exonic	misse
SF3B1	0.08	chr2:1982673	SNV	C	C/A	0	1571	AAT	14	p.Lys666Asn	c.1998G>T		exonic	misse
SRSF2	0.211	chr17:747329	SNV	G	G/T	0	256	CAC	1	p.Pro95His	c.284C>A	0.01	exonic	misse
SRSF2	0.075	chr17:747329	SNV	G	G/A	0.000359807	146	CTC	1	p.Pro95Leu	c.284C>T	0	exonic	misse
SRSF2	0.38	chr17:747329	SNV	G	G/C	0	1137	CGC	1	p.Pro95Arg	c.284C>G	0.05	exonic	misse
TET2	0.25	chr4:1061557	INDEL	TC	TC/T	0	982	TGG	3	p.Val218fs	c.651delC		exonic	frame
TET2	0.04	chr4:1061559	INDEL	TC	TC/T	3.67968E-06	1985	ATT	3	p.Asn275fs	c.822delC		exonic	frame
TET2	0.11	chr4:1061561	INDEL	TCAGGTTC	TCAGGTTC/T	6.61302E-09	188	GCA	3	p.Gly355fs	c.1064_1070delGTTCCAG		exonic	frame
TET2	0.05	chr4:1061562	INDEL	GC	GC/G	6.45922E-08	1988	CTA	3	p.Thr395fs	c.1182delC		exonic	frame
TET2	0.078	chr4:1061566	INDEL	CA	CA/C	2.3E-14	741	AGC	3	p.Lys513fs	c.1538delA		exonic	frame
TET2	0.10	chr4:1061567	INDEL	C	C/CA	0	1992	AGA	3	p.Glu537fs	c.1605_1606insA		exonic	frame
TET2	0.103	chr4:1061569	SNV	C	C/T	0	1492	TAA	3	p.Gln618Ter	c.1852C>T		exonic	nonse
TET2	0.27	chr4:1061572	SNV	C	C/T	0	568	TAA	3	p.Gln731Ter	c.2191C>T		exonic	nonse
TET2	0.06	chr4:1061575	SNV	C	C/T	7.25521E-08	763	TAG	3	p.Gln831Ter	c.2491C>T		exonic	nonse
TET2	0.17	chr4:1061580	INDEL	AC	AC/A	0	1989	CAA	3	p.Gln969fs	c.2902_2902delC		exonic	frame
TET2	0.26	chr4:1061581	SNV	C	C/T	0	1995	TAA	3	p.Gln1009Ter	c.3025C>T		exonic	nonse
TET2	0.041	chr4:1061625	INDEL	CTATTA	CTATTA/C	7.93688E-05	1516	AGA	4	p.Ile1160fs	c.3477_3481delTATTA		exonic	frame
TET2	0.10	chr4:1061640	INDEL	GGGATGTCC	GGGATGTCC/(	0	694	GTA	5	p.Gly1192fs	c.3574_3581delGGATGTCC		exonic	frame
TET2	0.10	chr4:1061640	INDEL	GGGATGTCC	GGGATGTCC/(	0	694	GTA	5	p.Gly1192fs	c.3574_3581delGGATGTCC		exonic	frame
TET2	0.14	chr4:1061647	SNV	G	G/A	0	1999	TAT	6	p.Cys1221Tyr	c.3662G>A	0	exonic	misse
TET2	0.04	chr4:1061807	INDEL	T	T/TG	0.001423771	1751	TGG	7	p.Cys1271fs	c.3812_3813insG		exonic	frame
TET2	0.15	chr4:1061807	SNV	A	A/G	0	2000	CGG	7	p.Gln1274Arg	c.3821A>G	0	exonic	misse
TET2	0.045	chr4:1061808	INDEL	AC	AC/A	3.86981E-07	1985	GTG	7	p.Cys1281fs	c.3840delC		exonic	frame
TET2	0.15	chr4:1061829	SNV	G	G/T	6.42259E-08	96	TAG	8	p.Glu1323Ter	c.3967G>T		exonic	nonse
TET2	0.16	chr4:1061829	INDEL	CAT	CAT/C	0	309	TAA	8	p.Tyr1337Ter	c.4011_4012delTA		exonic	nonse
TET2	0.07	chr4:1061830	INDEL	AG	AG/A	5.60015E-06	394	CAG	8	p.Gln1348fs	c.4044_4044delG		exonic	frame
TET2	0.04	chr4:1061907	SNV	C	C/T	0.0051511	1267	TGT	9	p.Arg1359Cys	c.4075C>T	0.08	exonic	misse
TET2	0.05	chr4:1061907	SNV	G	G/C	2.67553E-08	1189	CCT	9	p.Arg1359Pro	c.4076G>C	0	exonic	misse
TET2	0.091	chr4:1061908	SNV	C	C/A	0	1997	AAC	9	p.His1382Asn	c.4144C>A	0	exonic	misse
TET2	0.04	chr4:1061937	SNV	C	C/T	0.001137077	981	TGA	10	p.Arg1404Ter	c.4210C>T		exonic	nonse
TET2	0.06	chr4:1061939	SNV	C	C/T	1.3527E-11	1573	TGA	10	p.Arg1465Ter	c.4393C>T		exonic	nonse
TET2	0.15	chr4:1061939	INDEL	CA	CA/C	0	1997	CGC	10	p.Ser1485fs	c.4453_4453delA		exonic	frame
TET2	0.06	chr4:1061963	INDEL	TCAGA	TCAGA/T	3.70681E-09	860	GAG	11	p.Thr1554fs	c.4657_4660delCAGA		exonic	frame
TET2	0.07	chr4:1061966	**INDEL**	GTC	GTC/G	0	1980	GCC	11	p.Gln1654fs	c.4959_4960delTC		exonic	frame
TET2	0.06	chr4:1061966	INDEL	GTC	GTC/G	0	1977	GCC	11	p.Gln1654fs	c.4959_4960delTC		exonic	frame
TET2	0.279	chr4:1061966	SNV	C	C/T	0	1996	TAG	11	p.Gln1654Ter	c.4960C>T		exonic	nonse
TET2	0.12	chr4:1061967	SNV	C	C/A	5.1E-14	268	TAA	11	p.Tyr1679Ter	c.5037C>A		exonic	nonse
TET2	0.09	chr4:1061969	INDEL	T	T/TGAACATA	0	1996	AGA	11	p.His1757fs	c.5262_5263insGAACATA		exonic	frame
TET2	0.42	chr4:1061971	INDEL	AT	AT/A	0	1406	ATG	11	p.Leu1830fs	c.5488_5488delT		exonic	frame
TET2	0.065	chr4:1061972	INDEL	TG	TG/T	7.23169E-05	339	ATC	11	p.Asp1856fs	c.5566delG		exonic	frame
TET2	0.04	chr4:1061972	SNV	C	C/T	0.00050754	820	TAT	11	p.His1868Tyr	c.5602C>T	0	exonic	misse
TET2	0.08	chr4:1061973	SNV	A	A/G	1.24328E-10	572	GCC	11	p.Thr1884Ala	c.5650A>G	0	exonic	misse
TET2	0.24	chr4:1061973	SNV	A	A/G	0	1998	GCC	11	p.Thr1884Ala	c.5650A>G	0	exonic	misse
TET2	0.112	chr4:1061973	SNV	A	A/G	0	1807	GGG	11	p.Arg1891Gly	c.5671A>G	0	exonic	misse
TET2	0.43	chr4:1061973	SNV	A	A/G	0	1419	GGG	11	p.Arg1891Gly	c.5671A>G	0	exonic	misse
TET2	0.40	chr4:1061974	SNV	G	G/T	0	1572	TAG	11	p.Glu1931Ter	c.5791G>T		exonic	nonse
TP53	0.06	chr17:757840	SNV	C	C/T	0	2000	CAC	5	p.Arg175His	c.524G>A		exonic	misse
TP53	0.042	chr17:757845	SNV	G	G/A	2.26475E-06	2000	TGC	5	p.Arg158Cys	c.472C>T	0	exonic	misse
U2AF1	0.34	chr21:445147	SNV	T	T/G	0	2000	CCG	6	p.Gln157Pro	c.470A>C		exonic	misse

Supplemental Table 4. CH/subtypes group demographics (total N=359)

Variable	No CH (N=276)			CH (N=83)			VAF>0.1 (N=36) (vs. VAF≤0.1 or no mutation)			Mut>1 (N=11) (vs. Mut≤1 or no mutation)			*TET2* mutation (N=34)			*DNMT3A* mutation (N=32)		
	% male (n)			% male (n)			% male (n)			% male (n)			% male (n)			% male (n)		
Sex	33.7 (93)			36.1 (30)			38.9 (14)			54.5 (6)			50 (17)			25 (8)		
	mean (SD)	median (IQR)	range	mean (SD)	median (IQR)	range	mean (SD)	median (IQR)	range	mean (SD)	median (IQR)	range	mean (SD)	median (IQR)	range	mean (SD)	median (IQR)	range
Age (y)	80 (8)	81 (73-86)	65-97	82 (8) *	83 (75-88)	65-104	83 (7) *	84 (79-88)	65-97	86 (6) *	85 (80-87)	79-100	82 (8)	83 (79-88)	68-97	81 (9)	80 (76-86)	65-104
Hemoglobin (g/L)	131 (14)	133 (122-141)	84-166	129 (13)	127 (120-141)	100-160	129 (14)	128 (119-139)	100-160	120 (12) *	124 (110-132)	101-134	129 (14)	133 (120-141)	100-160	126 (13)	125 (119-139)	101-150
Platelets	219 (54)	217 (183-248)	91-471	219 (93)	196 (167-253)	18-746	224 (114)	200 (163-261)	78-746	176 (64)	166 (131-226) ^	78-298	203 (61)	193 (164-243)	78-392	224 (76)	201 (174-254)	101-408
Monocytes (x 10^9/L)	0.6 (0.2)	0.5 (0.5-0.7)	0.3-1.4	0.6 (0.2)	0.6 (0.5-0.8)	0.3-1.3	0.6 (0.2)	0.6 (0.5-0.8)	0.3-1.1	0.7 (0.2)	0.7 (0.4-0.8)	0.3-1.1	0.6 (0.2)	0.6 (0.4-0.8)	0.3-1.1	0.6 (0.2)	0.6 (0.5-0.7)	0.3-1.3
WBC (x 10^9 /L)	7 (1.8)	6.7 (5.8-7.7)	3.6-19.7	6.9 (2.1)	6.6 (5.3-8.1)	3-13.1	6.8 (1.9)	6.8 (5.2-8.1)	4.1-10.7	5.5 (1.3) *	5.2 (4.2-7.1)	4.1-7.5	6.7 (1.9)	6.5 (5.2-7.5)	3.6-11.5	7.2 (2.3)	7.1 (5.4-8.8)	3.9-13.1
ANC (x 10^9 /L)	4.5 (1.6)	4.3 (3.5-5.2)	1.6-16.2	4.5 (1.7)	4.3 (3.4-5.3)	0.4-10.3	4.5 (1.5)	4.5 (3.3-5.7)	0.4-7.8	4.1 (1.5)	3.5 (3-5.3)	2.6-7.4	4.4 (1.4)	4.2 (3.3-5.1)	1.7-7.8	4.7 (1.8)	4.5 (3.3-5.6)	2.4-10.3
ALC (x 10^9 /L)	1.6 (0.6)	1.6 (1.3-2)	0.3-3.7	1.6 (0.7)	1.4 (1.1-1.8)	0.5-4.5	1.5 (0.6)	1.4 (1-1.8)	0.8-2.9	1.1 (0.3) *	1 (1-1.2)	0.9-1.9	1.5 (0.7)	1.3 (1-1.8)	0.8-4.5	1.6 (0.7)	1.5 (1.2-1.8)	0.6-3.8
RDW (%)	14.3 (1.4)	14 (13.2-14.8)	12.3-21.2	14.4 (1.4)	14.1 (13.6-15)	11.9-19.1	14.8 (1.6) *	14.7 (13.8-15.2)	12.8-19.1	14.4 (1.1)	14.4 (13.6-15.1)	12.9-16.7	14.3 (1.1)	14.1 (13.6-14.9)	11.9-16.9	14 (1)	13.9 (13.5-14.8)	12.3-16.7
MCV (fl)	90.3 (5.7)	90.4 (87.2-93.7)	63.9-106.3	90.6 (4.8)	90.6 (87.3-94.3)	76.2-102.2	90.6 (5)	90.5 (87.1-93.7)	80.7-102.2	91.9 (4.5)	91.1 (88.5-94.9)	84.2-101.3	90.5 (4.6)	90.6 (87.1-92.8)	80.7-102.2	90.2 (4.8)	90.6 (88.1-93.5)	76.2-96.4
Retic Count (x 10^9 /L)	56 (19)	54 (44-66)	14-115	57 (21)	53 (40-68)	21-111	61 (22)	57 (44-77)	34-111	56 (21)	48 (44-66)	36-107	59 (21)	54 (44-74)	32-111	53 (19)	47 (38-64)	21-100
LDH (IU/L)	184 (38)	179 (160-205)	88-351	190 (36)	188 (165-207)	114-305	188 (33)	188 (170-207)	114-253	184 (15)	182 (170-196)	165-210	181 (30)	182 (158-205)	114-252	193 (36)	190 (170-206)	136-305
Ferritin (ug/L)	130.6 (107.9)	100.5 (53-180)	0.3-695	123.3 (102.6)	91 (50-176)	17-527	150.6 (136.1)	96.5 (52.5-218)	17-527	99.2 (69.5)	92 (43-111)	28-282	122.6 (97.3)	95 (58-162)	23-527	106.7 (72.7)	84.5 (43-178.5)	17-257
Iron (umol/L)	14 (5)	14 (10-17)	2-39	14 (5)	13 (10-17)	4-27	13 (5)	12 (10-16)	4-27	14 (3)	13 (10-17)	10-18	14 (5)	13 (11-17)	7-25	12 (4)	12 (10-14)	4-23
TIBC (Umol/L)	54 (10)	54 (48-59)	15-94	54 (10)	55 (47-60)	25-80	55 (9)	55 (49-60)	36-80	54 (8)	56 (47-59)	41-65	53 (8)	54 (48-58)	25-65	55 (11)	57 (44-61)	34-80
Vitamin B12 (pmol/L)	442 (291)	355 (255-525)	99-1476	414 (223)	372 (281-488)	55-1449	399 (228)	331 (278-485)	146-1449	341 (77)	343 (279-421)	218-453	443 (274)	370 (283-566)	55-1449	345 (144)	300 (268-408)	116-877
TSH (mIU/L)	2.3 (1.6)	2 (1.4-2.8)	0-15.5	3.1 (3.5)	2.2 (1.5-3.4) ^	0.4-27.8	3.8 (4.9)	2.3 (1.6-3.9) ^	0.5-27.8	3.4 (2.4)	2.5 (1.3-5.6)	0.4-7.6	3.8 (4.6)	2.6 (1.8-3.8) ^	0.5-27.8	2.5 (1.6)	2.4 (1.6-3.3)	0.4-9.5
CRP	4.5 (12.6)	2 (1-4)	0.5-152	5.5 (14.1)	2 (1-5)	0.5-95	6.6 (15.8)	2 (1-6)	0.5-95	1.6 (1.9)	1 (0.5-2) ^	0.5-7	3 (2.3)	2 (1-5)	0.5-9	9.4 (21.9)	3.5 (1-6)	0.5-95
AST (IU/L)	23 (8)	21 (18-25)	11-71	21 (6)	21 (18-23)	11-49	21 (6)	20 (17-23)	11-39	21 (6)	21 (15-25)	11-30	21 (6)	21 (18-24)	11-35	21 (7)	21 (18-23)	11-49
ALT(IU/L)	20 (10)	17 (14-23)	4-102	18 (8)	16 (13-22)	4-50	18 (10)	16 (13-22)	4-50	18 (9)	16 (13-21)	4-35	18 (8)	16 (13-21)	4-43	19 (8)	18 (14-22)	4-39
T bili (umol/L)	8.3 (5.7)	7 (5-10)	1.5-61	8.2 (4.2)	7 (5-10)	1.5-22	7.6 (3.3)	7 (5-9)	1.5-15	7.1 (1.9)	7 (6-9)	4-10	8.7 (4.4)	7 (7-10)	3-22	7.5 (3.8)	7 (5-10)	1.5-19
Creatinine (µmol/L)	86 (35)	80 (67-96)	42-428	92 (36)	81 (71-110)	47-307	94 (43)	87 (68-113)	56-307	99 (31)	106 (71-119)	57-154	95 (44)	85 (71-111)	47-307	94 (35)	81 (71-116)	47-192
Creatinine Clearence (ml/min)	60.6 (20.8)	60.7 (46.6-74)	8.2-143.3	57.3 (22.1)	57.6 (40-70)	24.4-126.8	57.2 (22.8)	57.4 (39.9-70.2)	26.3-126.8	51.3 (27.9)	42.6 (32.2-57.6) ^	25.9-126.8	59.1 (20.1)	57.8 (45.1-72)	27.6-126.8	55.6 (25.8)	55.4 (34.8-67)	24.4-116.1
Albumin (g/L)	43 (3)	43 (41-45)	31-50	43 (3)	44 (42-45)	31-51	43 (3)	43 (42-45)	38-50	43 (2)	43 (42-45)	38-46	44 (3)	44 (42-45)	38-49	43 (3)	43 (41-45)	31-48
Calcium (mmol/L)	2.4 (0.1)	2.4 (2.3-2.5)	2-2.8	2.4 (0.1)	2.4 (2.3-2.5)	2.2-2.7	2.4 (0.1)	2.4 (2.3-2.5)	2.2-2.7	2.4 (0.1)	2.4 (2.3-2.4)	2.3-2.5	2.4 (0.1)	2.4 (2.3-2.5)	2.2-2.6	2.4 (0.1)	2.4 (2.3-2.4)	2.2-2.6

* denotes <0.05 significance without correcting for multiple comparisons; ^ denotes signifiance with Mann-Whitney without correcting for multiple comparisons.

Supplemental Table 5. CH/subtypes and laboratory values

Lab item	Raw p-value	FDR adjusted p-value	Bonferroni adjusted p-value	OR	95%CI Lower	95%CI Upper
Any mutation (CH) vs. no mutation						
Albumin (g/L)	0.0689	0.0788	0.1378	1.091	0.995	1.201
TSH (mIU/L, log)	0.0856	0.0856	0.1712	1.418	0.962	2.136
Monocytes (x 10^9/L)	0.163	0.9065	0.3261	2.425	0.688	8.381
AST (IU/L, log)	0.25	0.9065	0.4999	0.595	0.241	1.418
Creatinine (µmol/L, log)	0.2828	0.9065	0.5657	1.547	0.688	3.417
LDH (IU/L)	0.283	0.9065	0.5661	1.004	0.997	1.01
Platelets (x 10^9/L, log)	0.299	0.9065	0.5981	0.661	0.297	1.456
Hemoglobin (g/L)	0.3177	0.9065	0.6354	0.991	0.973	1.009
ALT (IU/L, log)	0.3952	0.9065	0.7904	0.765	0.409	1.415
Iron (umol/L)	0.4517	0.9065	0.9035	1.02	0.968	1.075
CRP (log)	0.4748	0.9065	0.9496	1.085	0.865	1.353
WBC (x 10^9 /L)	0.6385	0.9065	0.992	0.968	0.844	1.103
ANC (x 10^9 /L)	0.7629	0.9065	0.992	0.976	0.827	1.137
ALC (x 10^9 /L)	0.6686	0.9065	0.992	0.915	0.6	1.364
RDW (%)	0.8124	0.9065	0.992	1.022	0.851	1.213
MCV (fl)	0.8277	0.9065	0.992	1.005	0.961	1.053
Retic Count (x 10^9 /L)	0.5645	0.9065	0.992	1.004	0.991	1.017
Ferritin (ug/L, log)	0.7571	0.9065	0.992	1.047	0.79	1.406
TIBC (Umol/L)	0.6148	0.9065	0.992	1.007	0.981	1.032
Vitamin B12 (pmol/L, log)	0.6061	0.9065	0.992	0.886	0.556	1.4
Total bilirubin (umol/L, log)	0.7436	0.9065	0.992	1.076	0.694	1.683
Creatinine clearence (ml/min, log)	0.992	0.992	0.992	1.004	0.485	2.12
Calcium (mmol/L)	0.8956	0.9363	0.992	1.159	0.124	10.418
VAF>0.1 vs. VAF<0.1 or no mutation						
TSH (mIU/L, log)	**0.0269**	**0.0381**	0.0539	1.876	1.083	3.308
Retic Count (x 10^9 /L)	0.0532	0.0532	0.1064	1.017	0.999	1.034
RDW (%)	0.0572	0.0572	0.1144	1.229	0.983	1.511
AST (IU/L, log)	0.1408	0.651	0.2816	0.385	0.104	1.324
Albumin (g/L)	0.1415	0.651	0.283	1.105	0.971	1.267
ALT (IU/L, log)	0.263	0.7821	0.526	0.606	0.251	1.45
Ferritin (ug/L, log)	0.2694	0.7821	0.5389	1.273	0.842	1.98
CRP (log)	0.2789	0.7821	0.5577	1.181	0.866	1.588
TIBC (Umol/L)	0.3241	0.7821	0.6483	1.018	0.983	1.054
ALC (x 10^9 /L)	0.34	0.7821	0.6801	0.743	0.39	1.325
Creatinine (µmol/L, log)	0.3794	0.7934	0.7589	1.623	0.523	4.599
Hemoglobin (g/L)	0.6552	0.8843	0.9862	0.994	0.97	1.02
Platelets (x 10^9/L, log)	0.8065	0.9448	0.9862	0.875	0.316	2.708
Monocytes (x 10^9/L)	0.5416	0.8843	0.9862	1.711	0.286	9.186
WBC (x 10^9 /L)	0.5625	0.8843	0.9862	0.945	0.772	1.133
ANC (x 10^9 /L)	0.652	0.8843	0.9862	0.949	0.744	1.172
MCV (fl)	0.9862	0.9862	0.9862	1.001	0.94	1.068
LDH (IU/L)	0.8216	0.9448	0.9862	1.001	0.992	1.01
Iron (umol/L)	0.9616	0.9862	0.9862	0.998	0.924	1.074
Vitamin B12 (pmol/L, log)	0.5535	0.8843	0.9862	0.823	0.427	1.557
Total bilirubin (umol/L, log)	0.6416	0.8843	0.9862	0.862	0.465	1.623
Creatinine clearence (ml/min, log)	0.6921	0.8843	0.9862	1.232	0.451	3.566
Calcium (mmol/L)	0.9434	0.9862	0.9862	1.119	0.047	23.901
Mutation count>1 vs. mutation count ≤1						
WBC (x 10^9 /L)	**0.006***	**0.0121***	**0.0121***	**0.508**	**0.3**	**0.793**
ALC (x 10^9 /L)	**0.0211***	**0.0211***	**0.0422***	**0.177**	**0.036**	**0.677**
Platelets (x 10^9/L, log)	**0.0378**	**0.0378**	0.0756	0.248	0.058	1.026
CRP (log)	**0.0431**	**0.0431**	0.0861	0.456	0.195	0.909
Hemoglobin (g/L)	**0.0446**	**0.0446**	0.0892	0.959	0.919	0.999
ANC (x 10^9 /L)	0.1951	0.7477	0.3901	0.73	0.436	1.12
Creatinine (µmol/L, log)	0.2679	0.7874	0.5358	2.651	0.396	13.025
TSH (mIU/L, log)	0.3587	0.7874	0.7174	1.531	0.639	3.747
Monocytes (x 10^9/L)	0.3624	0.7874	0.7247	3.726	0.186	56.414
Calcium (mmol/L)	0.3696	0.7874	0.7391	0.073	0	19.193
AST (IU/L, log)	0.3911	0.7874	0.7821	0.388	0.041	3.09
Vitamin B12 (pmol/L, log)	0.438	0.7874	0.876	0.636	0.198	1.957
Albumin (g/L)	0.445	0.7874	0.8901	1.094	0.88	1.389
RDW (%)	0.8045	0.8811	0.9642	0.946	0.571	1.396
MCV (fl)	0.5343	0.8192	0.9642	1.037	0.928	1.168
Retic Count (x 10^9 /L)	0.7455	0.8573	0.9642	1.005	0.972	1.035
LDH (IU/L)	0.71	0.8573	0.9642	0.997	0.979	1.012
Ferritin (ug/L, log)	0.8997	0.9406	0.9642	0.955	0.496	2.017
Iron (umol/L)	0.6714	0.8573	0.9642	1.027	0.898	1.153
TIBC (Umol/L)	0.9642	0.9642	0.9642	1.001	0.943	1.063
ALT (IU/L, log)	0.5147	0.8192	0.9642	0.595	0.127	2.794
Total bilirubin (umol/L, log)	0.7052	0.8573	0.9642	0.807	0.273	2.507
Creatinine clearence (ml/min, log)	0.6167	0.8573	0.9642	0.654	0.138	3.772
***TET2* mutation vs. no mutation**						
TSH (mIU/L, log)	**0.0063***	**0.0125***	**0.0125***	**2.247**	**1.267**	**4.06**
Platelets (x 10^9/L, log)	0.0618	0.0618	0.1237	0.282	0.075	1.077
Creatinine (µmol/L, log)	0.1206	0.7726	0.2412	2.283	0.776	6.25
AST (IU/L, log)	0.1899	0.7726	0.3798	0.421	0.109	1.491
ALT (IU/L, log)	0.2101	0.7726	0.4202	0.578	0.243	1.362
ALC (x 10^9 /L)	0.2581	0.7726	0.5163	0.701	0.363	1.265
Total bilirubin (umol/L, log)	0.3056	0.7726	0.6112	1.385	0.747	2.616
Monocytes (x 10^9/L)	0.314	0.7726	0.6279	2.445	0.402	13.262
Iron (umol/L)	0.3281	0.7726	0.6562	1.036	0.963	1.111
Albumin (g/L)	0.3461	0.7726	0.6922	1.064	0.938	1.217
Hemoglobin (g/L)	0.3916	0.7726	0.7831	0.989	0.966	1.014
Retic Count (x 10^9 /L)	0.4031	0.7726	0.8062	1.007	0.989	1.025
WBC (x 10^9 /L)	0.447	0.7909	0.8941	0.922	0.735	1.123
ANC (x 10^9 /L)	0.7737	0.9313	0.9732	0.966	0.74	1.197
RDW (%)	0.6972	0.9313	0.9732	1.049	0.808	1.313
MCV (fl)	0.9035	0.9682	0.9732	1.004	0.943	1.073
LDH (IU/L)	0.7482	0.9313	0.9732	0.998	0.988	1.008
Ferritin (ug/L, log)	0.8035	0.9313	0.9732	1.052	0.718	1.611
TIBC (Umol/L)	0.7616	0.9313	0.9732	0.994	0.958	1.032
Vitamin B12 (pmol/L, log)	0.9732	0.9732	0.9732	0.989	0.513	1.87
CRP (log)	0.9261	0.9682	0.9732	1.016	0.718	1.402
Creatinine clearence (ml/min, log)	0.8098	0.9313	0.9732	0.893	0.368	2.345
Calcium (mmol/L)	0.5315	0.8731	0.9732	0.37	0.015	7.857
***DNMT3A* mutation vs. no mutation**						
CRP (log)	0.0515	0.0515	0.1031	1.346	0.992	1.807
Hemoglobin (g/L)	0.0663	0.0663	0.1325	0.977	0.953	1.002
Creatinine clearence (ml/min, log)	0.0916	0.0916	0.1832	0.48	0.207	1.148
Monocytes (x 10^9/L)	0.13	0.4924	0.2601	3.786	0.639	20.3
Vitamin B12 (pmol/L, log)	0.1337	0.4924	0.2674	0.574	0.269	1.163
Creatinine (µmol/L, log)	0.1364	0.4924	0.2729	2.269	0.742	6.446
Iron (umol/L)	0.1498	0.4924	0.2997	0.942	0.866	1.02
LDH (IU/L)	0.1826	0.525	0.3652	1.006	0.997	1.015
AST (IU/L, log)	0.337	0.6204	0.674	0.525	0.132	1.887
Albumin (g/L)	0.3757	0.6204	0.7514	0.948	0.844	1.072
Retic Count (x 10^9 /L)	0.3802	0.6204	0.7603	0.991	0.97	1.01
ANC (x 10^9 /L)	0.3978	0.6204	0.7957	1.091	0.874	1.313
Ferritin (ug/L, log)	0.415	0.6204	0.8299	0.855	0.598	1.272
Calcium (mmol/L)	0.4219	0.6204	0.8437	0.265	0.009	6.373
TSH (mIU/L, log)	0.4478	0.6204	0.8956	1.264	0.703	2.384
WBC (x 10^9 /L)	0.4591	0.6204	0.9183	1.07	0.881	1.264
RDW (%)	0.468	0.6204	0.9359	0.899	0.651	1.171
Platelets (x 10^9/L, log)	0.9636	0.9636	0.9636	0.968	0.24	4.03
ALC (x 10^9 /L)	0.6278	0.7175	0.9636	0.861	0.453	1.544
MCV (fl)	0.856	0.8949	0.9636	0.994	0.934	1.064
TIBC (Umol/L)	0.5125	0.6204	0.9636	1.012	0.976	1.05
ALT (IU/L, log)	0.6551	0.7175	0.9636	0.82	0.338	1.964
Total bilirubin (umol/L, log)	0.4929	0.6204	0.9636	0.808	0.442	1.508

Supplemental Table 6. CH/subtypes and specific comorbidities

Any mutation (CH) vs. no mutation	N with comorbidity/ Total N		Raw p-value	FDR p-value	Bonferroni p-value	OR (95% CI)
	CH	No CH				
CPD, symptomatic	11/83	18/276	0.0608	0.0608	0.1825	2.159 (0.940, 4.770)
GERD	20/83	45/276	0.0697	0.0697	0.2092	1.753 (0.943, 3.188)
DB with EOD	12/83	22/276	0.1007	0.3724	0.302	1.888 (0.860, 3.977)
CPD, asymptomatic	4/83	6/276	0.1354	0.375	0.4062	2.716 (0.669, 9.981)
LD, mild	2/83	1/276	0.1368	0.375	0.4103	6.314 (0.590, 138.1)
CVD	15/83	34/276	0.2076	0.4801	0.6228	1.539 (0.769, 2.964)
VHD	10/83	19/276	0.2298	0.5001	0.6894	1.652 (0.703, 3.678)
DVT/PE	2/83	2/276	0.2529	0.5093	0.7588	3.181 (0.375, 27.03)
PUD	4/83	6/276	0.2615	0.5093	0.7846	2.116 (0.521, 7.718)
Angina/CABG	14/83	38/276	0.6908	0.9467	0.9585	1.148 (0.566, 2.219)
Arrhythmia	15/83	49/275	0.7741	0.9547	0.9585	0.909 (0.463, 1.706)
Arthritis	45/83	149/276	0.7192	0.9503	0.9585	0.912 (0.551, 1.511)
Cancer^	12/83	31/276	0.4461	0.7503	0.9585	1.325 (0.622, 2.673)
CHF	7/83	18/276	0.9132	0.9585	0.9585	1.053 (0.389, 2.573)
Dementia	6/83	15/276	0.6277	0.8933	0.9585	1.278 (0.439, 3.294)
DB, no EOD	12/83	46/276	0.5467	0.8794	0.9585	0.807 (0.388, 1.574)
LD, mod/severe	1/83	1/276	0.3577	0.6305	0.9585	3.695 (0.145, 94.16)
MI	6/83	27/276	0.3578	0.6305	0.9585	0.647 (0.233, 1.539)
PVD	3/83	11/276	0.9585	0.9585	0.9585	0.966 (0.213, 3.230)
RD, mild	8/83	21/276	0.5762	0.8883	0.9585	1.278 (0.512, 2.917)
RD, mod/severe	15/83	46/276	0.6118	0.8933	0.9585	0.839 (0.415, 1.623)
Rheumatic disease	3/83	10/276	0.8886	0.9585	0.9585	0.910 (0.200, 3.076)

VAF>0.1 vs. VAF<0.1 or no mutation	N with comorbidity/ Total N		Raw p-value	FDR p-value	Bonferroni p-value	OR (95% CI)
	VAF>0.1	VAF<0.1 or no mutation				
DB with EOD	7/36	27/323	**0.0477**	**0.0477**	0.143	2.547 (0.945, 6.166)
LD, mod/severe	1/36	1/323	0.0962	0.0962	0.2887	10.775 (0.418, 278)
VHD	6/36	23/323	0.1011	0.4331	0.3032	2.284 (0.784, 5.828)
CVD	8/36	41/323	0.1336	0.4355	0.4007	1.929 (0.772, 4.387)
RD, mild	5/36	24/323	0.1875	0.4791	0.5625	2.012 (0.639, 5.326)
GERD	9/36	56/323	0.1942	0.4791	0.5827	1.720 (0.723, 3.787)
Angina/CABG	5/36	47/323	0.7135	0.8528	0.9914	0.828 (0.269, 2.097)
Arrhythmia	6/36	58/322	0.6319	0.8254	0.9914	0.796 (0.286, 1.900)
Arthritis	22/36	172/323	0.5737	0.8148	0.9914	1.228 (0.605, 2.564)
Cancer^	4/36	39/323	0.8454	0.9464	0.9914	0.896 (0.256, 2.434)
CPD, asymptomatic	1/36	9/323	0.8557	0.9464	0.9914	1.217 (0.064, 6.992)
CPD, symptomatic	3/36	26/323	0.9881	0.9914	0.9914	0.990 (0.226, 3.058)
CHF	4/36	21/323	0.5824	0.8148	0.9914	1.384 (0.377, 4.038)
Dementia	1/36	20/323	0.3759	0.6322	0.9914	0.397 (0.022, 2.020)
DB, no EOD	7/36	51/323	0.647	0.8254	0.9914	1.230 (0.472, 2.838)
DVT/PE	1/36	3/323	0.3689	0.6322	0.9914	2.871 (0.139, 23.37)
LD, mild	0/36	3/323	0.9914	0.9914	0.9914	1.256 (0.009, 13.31)
MI	3/36	30/323	0.7145	0.8528	0.9914	0.792 (0.182, 2.408)
PUD	1/36	9/323	0.8975	0.9488	0.9914	0.870 (0.046, 5.007)
PVD	2/36	12/323	0.5148	0.7936	0.9914	1.677 (0.251, 6.657)
RD, mod/severe	6/36	55/323	0.4498	0.7235	0.9914	0.689 (0.240, 1.709)
Rheumatic disease	2/36	11/323	0.5946	0.8148	0.9914	1.525 (0.229, 6.028)

Mutation count>1 vs. mutation count ≤1	N with comorbidity/ Total N		Raw p-value	FDR p-value	Bonferroni p-value	OR (95% CI)
	Mut>1	Mut≤1				
DB with EOD	5/11	29/348	**0.0008***	**0.0023***	**0.0023***	8.835 (2.364, 31.91)
CPD, asymptomatic	2/11	8/348	**0.0028***	**0.0042***	**0.0084***	16.691 (2.095, 102)
CVD	3/11	46/348	0.2028	0.9925	0.6084	2.447 (0.516, 8.971)
RD, mod/severe	1/11	60/348	0.2148	0.9925	0.6444	0.260 (0.014, 1.502)
CPD, symptomatic	2/11	27/348	0.2806	0.9925	0.8418	2.431 (0.350, 10.4)
PVD	1/11	13/348	0.3077	0.9925	0.9232	3.098 (0.159, 19.5)
Angina/CABG	1/11	51/348	0.4661	0.9925	0.9925	0.458 (0.024, 2.541)
Arrhythmia	3/11	61/347	0.5796	0.9925	0.9925	1.472 (0.313, 5.318)
Arthritis	7/11	187/348	0.7594	0.9925	0.9925	1.220 (0.352, 4.810)
Cancer^	2/11	41/348	0.531	0.9925	0.9925	1.658 (0.245, 6.848)
CHF	2/11	23/348	0.3764	0.9925	0.9925	2.089 (0.298, 9.163)
DB, no EOD	2/11	56/348	0.9234	0.9925	0.9925	1.080 (0.161, 4.392)
GERD	1/11	64/348	0.4941	0.9925	0.9925	0.483 (0.026, 2.635)
MI	1/11	32/348	0.8773	0.9925	0.9925	0.848 (0.045, 4.720)
PUD	1/11	9/348	0.3406	0.9925	0.9925	3.004 (0.145, 20.41)
RD, mild	1/11	28/348	0.8695	0.9925	0.9925	1.193 (0.063, 6.748)
VHD	1/11	28/348	0.9147	0.9925	0.9925	0.891 (0.047, 5.050)
Dementia	0/11	21/348	NA			
DVT/PE	0/11	4/348	NA			
LD, mild	0/11	3/348	NA			
LD, mod/severe	0/11	2/348	NA			
Rheumatic disease	0/11	13/348	NA			

TET2 mutation vs. no mutation	N with comorbidity/ Total N		Raw p-value	FDR p-value	Bonferroni p-value	OR (95% CI)
	TET2	No mut				
CPD, asymptomatic	3/34	6/276	**0.0343**	**0.0343**	0.103	4.626 (1.057, 17.2)
DB with EOD	6/34	22/276	0.0553	0.0553	0.1659	2.580 (0.925, 6.422)
LD, mild	1/34	1/276	0.1394	0.737	0.4183	8.228 (0.654, 103.5)
DVT/PE	1/34	2/276	0.187	0.7375	0.5611	4.914 (0.440, 38.09)
CPD, symptomatic	4/34	18/276	0.205	0.7375	0.6149	2.061 (0.610, 5.745)
Angina/CABG	7/34	38/276	0.2451	0.7375	0.7353	1.689 (0.660, 3.897)
RD, mod/severe	3/34	46/276	0.3132	0.7375	0.9395	0.551 (0.145, 1.540)
Arrhythmia	6/34	49/275	0.927	0.9715	0.9715	1.044 (0.389, 2.446)
Arthritis	16/34	149/276	0.448	0.7375	0.9715	0.761 (0.373, 1.541)
Cancer^	5/34	31/276	0.4616	0.7375	0.9715	1.453 (0.493, 3.646)
CVD	4/34	34/276	0.9466	0.9715	0.9715	1.037 (0.317, 2.728)
CHF	3/34	18/276	0.482	0.7375	0.9715	1.553 (0.393, 4.657)
Dementia	1/34	15/276	0.7549	0.8729	0.9715	0.755 (0.081, 3.199)
DB, no EOD	7/34	46/276	0.4991	0.7375	0.9715	1.352 (0.533, 3.083)
GERD	7/34	45/276	0.4632	0.7375	0.9715	1.387 (0.546, 3.168)
LD, mod/severe	0/34	1/276	0.6745	0.8472	0.9715	2.649 (0.018, 50.91)
MI	4/34	27/276	0.5967	0.7886	0.9715	1.339 (0.406, 3.581)
PUD	1/34	6/276	0.528	0.7375	0.9715	1.863 (0.190, 9.255)
PVD	1/34	11/276	0.9715	0.9715	0.9715	1.033 (0.110, 4.556)
RD, mild	2/34	21/276	0.8991	0.9715	0.9715	0.914 (0.178, 3.030)
Rheumatic disease	1/34	10/276	0.8905	0.9715	0.9715	1.137 (0.120, 5.083)
VHD	3/34	19/276	0.5382	0.7375	0.9715	1.467 (0.373, 4.374)

DNMT3A mutation vs. no mutation	N with comorbidity/ Total N		Raw p-value	FDR p-value	Bonferroni p-value	OR (95% CI)
	DNMT3A	No mut				
GERD	12/32	45/276	**0.0043***	**0.0064***	**0.0129***	3.102 (1.404, 6.653)
CPD, symptomatic	6/32	18/276	**0.0154***	**0.0154***	**0.0461***	3.427 (1.206, 8.794)
CPD, asymptomatic	3/32	6/276	**0.0276**	**0.0276**	0.0829	4.940 (1.126, 18.43)
DB with EOD	6/32	22/276	**0.0401**	**0.0401**	0.1204	2.774 (0.990, 6.952)
PUD	2/32	6/276	0.1311	0.4042	0.3932	3.409 (0.606, 14.06)
DVT/PE	1/32	2/276	0.1709	0.4216	0.5127	5.225 (0.468, 40.57)
DB, no EOD	2/32	46/276	0.1877	0.4293	0.5632	0.406 (0.081, 1.287)
VHD	4/32	19/276	0.1972	0.4293	0.5917	2.085 (0.618, 5.802)
CVD	6/32	34/276	0.2555	0.4555	0.7664	1.724 (0.631, 4.158)
RD, mild	4/32	21/276	0.2649	0.4555	0.7948	1.876 (0.559, 5.165)
Dementia	3/32	15/276	0.2771	0.4555	0.8313	2.001 (0.500, 6.168)
Arrhythmia	8/32	49/275	0.2832	0.4555	0.8495	1.588 (0.652, 3.555)
Angina/CABG	4/32	38/276	0.967	0.9749	0.9749	0.978 (0.299, 2.569)
Arthritis	20/32	149/276	0.3771	0.5366	0.9749	1.399 (0.674, 3.011)
Cancer^	4/32	31/276	0.7057	0.8159	0.9749	1.230 (0.374, 3.275)
CHF	2/32	18/276	0.8505	0.9255	0.9749	1.145 (0.221, 3.869)
LD, mild	0/32	1/276	0.6566	0.8159	0.9749	2.806 (0.019, 54.11)
LD, mod/severe	0/32	1/276	0.6566	0.8159	0.9749	2.806 (0.019, 54.11)
MI	2/32	27/276	0.6712	0.8159	0.9749	0.743 (0.146, 2.425)
PVD	1/32	11/276	0.9182	0.9706	0.9749	1.099 (0.117, 4.860)
RD, mod/severe	7/32	46/276	0.4011	0.5497	0.9749	1.458 (0.571, 3.351)
Rheumatic disease	2/32	10/276	0.3338	0.494	0.9749	2.079 (0.388, 7.629)

^One of: Leukemia, lymphoma, other hematologic malignancy, solid tumour without metastasis, solid tumour with metastasis

Angina/coronary artery bypass graft (angina/CABG), cerebrovascular disease (CVD), congestive heart failure (CHF), deep vein thrombosis/pulmonary embolism (DVT/PE), diabetes with/no end organ damage (DB with/no EOD), gastroesophageal reflux disease (GERD), myocardial infarction (MI), peptic ulcer disease (PUD), peripheral vascular disease (PVD), valvular heart disease (VHD).

Supplemental Table 7. CH/subtypes and cytokine values

Any mutation (CH) vs. no mutation

Cytokine	Raw p-value	FDR-adjusted p-value	Bonferroni-adjusted p-value	OR (95% CI)	Median (IQR) No CH ^	Median (IQR) CH ^	Median (IQR) No CH ^^	Median (IQR) CH ^^
TNFα	0.0535	0.0951	0.2139	1.014 (1.000, 1.028)	22.3 (12.5-35.2)	26.7 (18.6-43.6)	17.5 (12.6-25.7)	20.4 (15.7-31.8)
IL-6	0.0987	0.0987	0.3947	1.013 (0.997, 1.029)	2.7 (0.5-6.5)	5.2 (1-11.8)	1.5 (0.3-3.6)	2.3 (0.7-5.1)
MCP-1/CCL2	0.0861	0.0951	0.3442	1.011 (0.998, 1.024)	35.4 (24.2-48.3)	38.3 (23.3-61.3)	434.9 (334.4-580.9)	465.4 (338.8-589.9)
Eotaxin1	0.1228	0.9984	0.4913	1.010 (0.997, 1.024)	30.2 (19.2-43.7)	34.8 (23.1-46.4)	118 (77.7-163.3)	148.9 (87.2-204.1)
IL-8	0.1396	0.9984	0.5582	1.010 (0.996, 1.023)	5.5 (2.3-13.6)	7 (2.9-19.6)	17.9 (10.3-35.7)	22.6 (11.9-41.6)
IL-7	0.1602	0.9984	0.6407	1.009 (0.996, 1.021)	11.6 (4.2-25.1)	17.2 (5.8-32)	2.8 (1.4-4.6)	2.7 (1.5-6.1)
G-CSF	0.2257	0.9984	0.9028	1.009 (0.994, 1.024)	1.1 (0.4-9.7)	1.5 (0.4-19.9)	3.2 (1.4-34.7)	4 (1.3-46.1)
IP-10/CXCL10	0.3	0.9984	0.9984	1.008 (0.992, 1.024)	9.2 (4.7-17.5)	11.7 (5.9-25.3)	125.3 (79.9-202.3)	145.8 (88-266.5)
IL-9	0.3826	0.9984	0.9984	1.007 (0.991, 1.021)	1.6 (0.5-4.7)	1.8 (0.8-4.9)	0.4 (0.2-1)	0.4 (0.2-2.1)
IL-4	0.4002	0.9984	0.9984	1.007 (0.989, 1.024)	2 (0-3.7)	2.3 (0.5-3.7)	0.6 (0.2-3.6)	1 (0.5-4.4)
MIP-1α	0.3026	0.9984	0.9984	1.006 (0.994, 1.019)	0.6 (0-8.1)	0.5 (0-13.9)	8.3 (0.6-20.8)	9 (0.6-19)
TGF-α	0.506	0.9984	0.9984	1.006 (0.986, 1.024)	0.8 (0.1-2)	0.9 (0.3-2.6)	3.5 (1.2-7.3)	3.2 (1.5-6.7)
IL-18	0.4004	0.9984	0.9984	1.005 (0.993, 1.018)	13.1 (6.1-28.2)	13.1 (6.7-33)	107.4 (38.8-205)	130.7 (42.9-236.8)
IL-1α	0.511	0.9984	0.9984	1.005 (0.988, 1.020)	0.2 (0-2.3)	0.2 (0-3.6)	2.6 (0.1-27.7)	3.2 (0.6-41.4)
IL-10	0.5687	0.9984	0.9984	1.005 (0.987, 1.022)	1.4 (0.1-4.4)	1.7 (0-4.3)	1.6 (0.4-4.2)	2 (0.2-4.8)
IL-17A	0.6167	0.9984	0.9984	1.005 (0.984, 1.024)	0.3 (0-2)	0.6 (0.1-3.2)	1.8 (0.6-9.1)	2.6 (0.6-13.3)
MDC	0.5973	0.9984	0.9984	1.004 (0.989, 1.019)	22 (14.2-36)	25.8 (15.1-33.2)	784.1 (488.8-1218.3)	703.8 (513.8-1189.6)
GM-CSF	0.7167	0.9984	0.9984	1.004 (0.980, 1.023)	0.9 (0.3-3)	1.1 (0.2-4.9)	5.7 (1.9-29.6)	7.7 (2.1-42.9)
PDGF-AA	0.5628	0.9984	0.9984	1.003 (0.992, 1.014)	22.9 (14.2-38.8)	21.5 (13.5-40.2)	1408.8 (1039.3-2074.2)	1449.2 (930.9-2384.8)
FGF-2	0.6396	0.9984	0.9984	1.003 (0.990, 1.016)	26.9 (8.6-38.7)	23.7 (7.7-39.8)	79.2 (57.8-97.8)	84.5 (59.3-109.6)
IL-5	0.8925	0.9984	0.9984	1.001 (0.983, 1.017)	0.7 (0.1-4)	0.7 (0.1-3.8)	0.2 (0-0.8)	0.2 (0-0.8)
Fractalkine	0.9429	0.9984	0.9984	1.001 (0.983, 1.016)	0 (0-1.3)	0 (0-1.6)	0.6 (0.6-18.3)	0.7 (0.6-27.8)
IFNa2	0.9296	0.9984	0.9984	1.001 (0.979, 1.018)	0.1 (0-2)	0.1 (0-4.9)	0.6 (0.1-16)	1.5 (0.1-31)
sCD40L	0.9984	0.9984	0.9984	1.000 (0.989, 1.011)	20.8 (7.6-42.4)	19.6 (7.1-44.1)	1470.3 (421.5-3151.8)	1633.1 (451.5-3271.6)
RANTES	0.9596	0.9984	0.9984	1.000 (0.987, 1.011)	11.4 (5.4-22.3)	12.7 (5.4-27)	384.4 (188.8-893.3)	371.1 (206.1-800.9)
IL-3	0.9949	0.9984	0.9984	1.000 (0.977, 1.019)	4.5 (0.9-9)	4.9 (1.8-9.8)	0.5 (0.4-0.6)	0.5 (0.4-0.8)
IL-12 p40	0.9788	0.9984	0.9984	1.000 (0.976, 1.018)	0.1 (0-1.8)	0.1 (0-4.3)	0.6 (0.6-17.1)	0.6 (0.6-29.7)
EGF	0.8087	0.9984	0.9984	0.999 (0.987, 1.010)	16.4 (2.2-31.9)	11 (3.8-34.3)	55.2 (11.8-137.6)	43.7 (17.1-132.3)
IL-13	0.9408	0.9984	0.9984	0.999 (0.984, 1.013)	0 (0-2.3)	0 (0-0.2)	0.7 (0.6-5)	0.7 (0.6-1.1)
Flt-3L	0.9192	0.9984	0.9984	0.999 (0.983, 1.014)	0 (0-11.4)	0 (0-8.6)	0.6 (0.6-28.9)	0.6 (0.1-34.9)
IL-1RA	0.8724	0.9984	0.9984	0.999 (0.982, 1.013)	1.8 (0-7.2)	1.8 (0-5.5)	14.2 (0.6-73.1)	13 (0.6-50.9)
GROa	0.8882	0.9984	0.9984	0.999 (0.981, 1.014)	10.2 (6.5-17)	10 (7.5-14.8)	1056.8 (716-1493.7)	1197.1 (856.5-1851)
VEGF-A	0.8302	0.9984	0.9984	0.998 (0.982, 1.014)	10 (4.2-17.8)	9.1 (2.8-21.4)	121.4 (62.5-206)	118.4 (46.2-235)
IL-15	0.8181	0.9984	0.9984	0.998 (0.979, 1.014)	3.2 (0.6-10.1)	2.8 (0.4-12)	1.6 (0.8-3.4)	2.1 (0.5-3.7)
IFNγ	0.8741	0.9984	0.9984	0.998 (0.977, 1.016)	0.8 (0-2.9)	0.8 (0-2.4)	3.1 (0.3-8.3)	2.5 (0.3-8.5)
IL-1β	0.8025	0.9984	0.9984	0.998 (0.977, 1.015)	0 (0-1.9)	0.3 (0-3.7)	0.6 (0.1-1.9)	0.6 (0.1-2.7)
IL-12 p70	0.704	0.9984	0.9984	0.997 (0.976, 1.013)	0 (0-1.1)	0 (0-1.4)	0.6 (0.2-3.5)	0.6 (0.2-4.6)
MCP-3/CCL7	0.5905	0.9984	0.9984	0.996 (0.980, 1.010)	0 (0-4.9)	0 (0-3.4)	0.6 (0.6-37.2)	0.6 (0.6-18.7)
TNFβ	0.6324	0.9984	0.9984	0.996 (0.978, 1.011)	0 (0-0)	0 (0-0.2)	0.6 (0.6-2.3)	0.6 (0.6-2.9)
PDGF-BB	0.3288	0.9984	0.9984	0.995 (0.985, 1.005)	17.6 (11.3-61.5)	19.1 (10.9-39.3)	5339.3 (3657.5-14915.5)	5162.3 (3539.9-12396.3)
IL-2	0.5592	0.9984	0.9984	0.993 (0.965, 1.013)	0.1 (0-2.1)	0 (0-2)	0.5 (0-1.9)	0.3 (0-1.1)
MIP-1β	0.3759	0.9984	0.9984	0.992 (0.975, 1.008)	12.9 (5.5-23.4)	11.7 (2.4-23)	44.3 (20-71.2)	49.6 (15.6-72.7)

VAF>0.1 vs. VAF<0.1 or no mutation

Cytokine	Raw p-value	FDR-adjusted p-value	Bonferroni-adjusted p-value	OR (95% CI)	Median (IQR) VAF<0.1 or no mutation ^	Median (IQR) VAF>0.1 ^	Median (IQR) VAF<0.1 or no mutation ^^	Median (IQR) VAF>0.1 ^^
TNFα	**0.0206**	**0.0413**	0.0825	1.020 (1.003, 1.038)	22.9 (13.6-35.4)	33.2 (17.1-51)	17.9 (12.7-25.7)	22.9 (16.4-32.4)
IL-6	0.6357	0.9966	0.9966	1.005 (0.980, 1.024)	2.7 (0.5-7.3)	5.1 (1.6-11.7)	1.5 (0.3-4)	2.3 (0.8-5)
MCP-1/CCL2	0.936	0.9966	0.9966	0.999 (0.981, 1.017)	37 (24.8-50)	35.1 (22.3-54.8)	433.5 (328.3-590.4)	492.9 (354.9-566.6)
Eotaxin1	0.5326	0.9966	0.9966	1.006 (0.987, 1.023)	31.6 (20-44.2)	33.4 (21.5-45.2)	121.1 (78.4-173.2)	146.4 (92.9-191.9)
IL-8	0.3469	0.9966	0.9966	1.008 (0.989, 1.025)	5.6 (2.3-14)	6.4 (3.7-18.4)	18.1 (10.3-35.8)	23.8 (12.5-38.8)
IL-7	0.4041	0.9966	0.9966	1.007 (0.989, 1.023)	12.5 (4.2-25.7)	17.8 (8.7-29)	2.7 (1.3-4.7)	3 (2-5.4)
G-CSF	0.4266	0.9966	0.9966	1.008 (0.986, 1.026)	1.2 (0.4-11)	1.6 (0.7-20.8)	3.3 (1.3-35.5)	5 (2-47.9)
IP-10/CXCL10	0.116	0.9966	0.4639	1.015 (0.995, 1.034)	9.3 (4.7-18.6)	12.1 (6.2-33.5)	126 (79.6-202.7)	150.8 (89.5-317.1)
IL-9	0.9834	0.9966	0.9966	1.000 (0.973, 1.020)	1.6 (0.6-4.9)	1.9 (0.4-4.8)	0.4 (0.2-1)	0.5 (0.3-2.1)
IL-4	0.4444	0.9966	0.9966	1.008 (0.983, 1.027)	1.9 (0-3.7)	2.3 (1.3-3.7)	0.6 (0.2-3.6)	1.3 (0.6-4.8)
MIP-1α	0.3793	0.9966	0.9966	1.007 (0.990, 1.022)	0.6 (0-10.4)	0.4 (0-13.4)	8.3 (0.6-20.2)	7.6 (0.6-19.8)
TGF-α	0.6681	0.9966	0.9966	1.005 (0.973, 1.026)	0.8 (0.1-2)	0.8 (0.2-2.6)	3.4 (1.2-7.3)	3.3 (1.8-6.5)
IL-18	**0.0129**	**0.0413**	0.0517	1.019 (1.003, 1.034)	12.7 (6.1-28.1)	17.5 (9.3-47.6)	107.7 (37.7-206.3)	152.6 (51.9-281.2)
IL-1α	0.0977	0.0977	0.3907	1.014 (0.995, 1.031)	0.2 (0-2.5)	0.2 (0-1.7)	3.1 (0.1-29.6)	3.2 (0.6-41.9)
IL-10	0.7921	0.9966	0.9966	1.003 (0.975, 1.023)	1.5 (0.1-4.4)	1.9 (0.5-4)	1.6 (0.2-4.3)	2 (0.6-4.8)
IL-17A	0.8728	0.9966	0.9966	0.998 (0.958, 1.022)	0.3 (0-1.9)	0.9 (0.3-3.8)	1.7 (0.5-9.1)	3.9 (1.1-15.2)
MDC	0.5134	0.9966	0.9966	0.992 (0.968, 1.014)	22.4 (14.8-36.6)	22.1 (13.3-32)	772.6 (495.4-1216.8)	696.8 (505.1-1283.6)
GM-CSF	0.9537	0.9966	0.9966	1.001 (0.960, 1.026)	0.9 (0.3-3.3)	1.1 (0.3-5.8)	6 (1.9-32.8)	7.8 (2.9-38.6)
PDGF-AA	0.9868	0.9966	0.9966	1.000 (0.984, 1.014)	22.9 (14.4-38.8)	17.5 (10.5-44.1)	1453.7 (1038.9-2134.2)	1252.5 (855.9-2195)
FGF-2	0.4271	0.9966	0.9966	1.007 (0.989, 1.024)	26.1 (8.4-39.1)	24.5 (8.3-41.4)	79.6 (57-99)	82.7 (65.2-112.8)
IL-5	0.9726	0.9966	0.9966	1.000 (0.972, 1.020)	0.7 (0.1-4)	0.2 (0.1-3.7)	0.2 (0-0.8)	0.1 (0-0.9)
Fractalkine	0.5857	0.9966	0.9966	1.005 (0.983, 1.022)	0 (0-1.3)	0.1 (0-2.7)	0.6 (0.6-19.5)	4.8 (0.6-102.7)
IFNa2	0.3107	0.9966	0.9966	1.010 (0.986, 1.029)	0 (0-2.4)	0.2 (0-2.4)	0.6 (0.1-20)	2.3 (0.3-28.7)
sCD40L	0.9556	0.9966	0.9966	1.000 (0.984, 1.014)	20.7 (7.6-42.7)	13 (7-44.3)	1555.4 (436.2-3251.7)	1031.9 (394.8-3151.5)
RANTES	0.9575	0.9966	0.9966	1.000 (0.982, 1.015)	11.5 (5.4-23.7)	12.3 (3.6-27.1)	373.2 (178.7-860.4)	409.8 (262.9-957.3)
IL-3	0.4949	0.9966	0.9966	0.986 (0.935, 1.016)	4.9 (1.2-9.4)	3.9 (1.2-7.6)	0.5 (0.4-0.6)	0.5 (0.4-0.8)
IL-12 p40	0.5738	0.9966	0.9966	1.007 (0.978, 1.027)	0.1 (0-2.1)	0.1 (0-2.1)	0.6 (0.5-20)	0.6 (0.6-27.3)
EGF	0.5617	0.9966	0.9966	1.004 (0.989, 1.019)	15.4 (3.2-31.6)	13.4 (3-40.6)	53.1 (14-133.9)	53.3 (7.1-186.3)
IL-13	0.996	0.9966	0.9966	1.000 (0.977, 1.017)	0 (0-2.1)	0 (0-0.2)	0.7 (0.6-4.5)	0.7 (0.6-0.7)
Flt-3L	0.6347	0.9966	0.9966	1.005 (0.983, 1.023)	0 (0-11.4)	0 (0-6.2)	0.6 (0.1-31.6)	0.6 (0.6-17.1)
IL-1RA	0.9761	0.9966	0.9966	1.000 (0.976, 1.018)	1.8 (0-7.2)	1.4 (0-4.9)	14.2 (0.6-71.7)	13.3 (1.2-43.5)
GROa	0.3971	0.9966	0.9966	1.008 (0.987, 1.026)	9.7 (6.7-16.1)	11.7 (8.5-21.2)	1066.1 (730.2-1500.1)	1407.1 (789.2-1999.4)
VEGF-A	0.3237	0.9966	0.9966	0.987 (0.959, 1.010)	10.1 (4-18.7)	8.2 (2.9-17.9)	122.3 (60.7-213.3)	101.8 (44.3-204.9)
IL-15	0.6833	0.9966	0.9966	1.004 (0.979, 1.024)	3 (0.6-9.7)	4.2 (0.7-15.9)	1.7 (0.6-3.6)	2.3 (1.3-3.6)
IFNγ	0.9966	0.9966	0.9966	1.000 (0.968, 1.021)	0.8 (0-2.7)	0.7 (0.1-2.8)	3.1 (0.3-8.2)	2.2 (0.6-9.2)
IL-1β	0.8526	0.9966	0.9966	0.998 (0.965, 1.019)	0 (0-1.9)	0.7 (0-4.7)	0.6 (0.1-2.1)	0.7 (0.5-2.8)
IL-12 p70	0.8313	0.9966	0.9966	1.002 (0.976, 1.021)	0 (0-1.2)	0 (0-2.7)	0.6 (0.2-3.5)	0.6 (0.2-4.5)
MCP-3/CCL7	0.9477	0.9966	0.9966	0.999 (0.977, 1.016)	0 (0-4.9)	0 (0-0.8)	0.6 (0.6-37.2)	0.6 (0.6-12.5)
TNFβ	0.8055	0.9966	0.9966	1.002 (0.980, 1.019)	0 (0-0.1)	0 (0-0)	0.6 (0.6-3.2)	0.6 (0.6-0.6)
PDGF-BB	0.2601	0.9966	0.9966	1.007 (0.994, 1.020)	17.4 (11.2-61.5)	26.7 (11.9-61.5)	5268.5 (3580.6-14280.4)	5818.2 (3879-21217.9)
IL-2	0.6693	0.9966	0.9966	1.005 (0.975, 1.025)	0.1 (0-2.1)	0.1 (0-2.1)	0.4 (0-1.8)	0.6 (0-2.6)
MIP-1β	0.1961	0.9966	0.7843	1.012 (0.992, 1.029)	12.4 (4.9-22.1)	20.3 (7.9-27.3)	42.7 (18.3-70.3)	59.6 (43.7-76.5)

Mutation count>1 vs. mutation count ≤1

Cytokine	Raw p-value	FDR-adjusted p-value	Bonferroni-adjusted p-value	OR (95% CI)	Median (IQR) Mutation count ≤1 ^	Median (IQR) Mutation count>1 ^	Median (IQR) Mutation count≤1 ^^	Median (IQR) Mutation count>1 ^^
TNFα	0.821	0.8898	0.9992	1.004 (0.964, 1.037)	23.9 (13.8-36.3)	23.4 (16.6-38.3)	18.5 (13-26)	22.9 (16.8-33.5)
IL-6	**0.008***	**0.0112***	**0.0319***	**1.031 (1.005, 1.054)**	2.7 (0.6-7.3)	9.1 (5.4-42.5)	1.5 (0.4-4.1)	4.2 (2.8-45.9)
MCP-1/CCL2	0.9992	0.9992	0.9992	1.000 (0.963, 1.033)	36.8 (23.9-50.5)	32.5 (11.1-56.7)	438 (335.3-586.9)	504.5 (343.6-551.7)
Eotaxin1	0.6215	0.791	0.9992	1.008 (0.972, 1.040)	32 (20.1-44.2)	26.5 (20.7-45.7)	122.9 (81.3-175.4)	122.9 (80-293.5)
IL-8	**0.0177**	**0.0177**	0.0707	1.029 (1.002, 1.052)	5.9 (2.5-13.9)	11.4 (3.4-55.3)	18.2 (10.7-35.8)	31.9 (20.4-95.7)
IL-7	0.4192	0.6521	0.9992	1.012 (0.978, 1.038)	12.8 (4.5-26.2)	20 (10.7-41.4)	2.7 (1.4-4.7)	4 (2.9-6.1)
G-CSF	**0.0063***	**0.0112***	**0.0252***	**1.037 (1.008, 1.064)**	1.2 (0.4-10.4)	18.7 (2.4-34.5)	3.3 (1.3-34.7)	52.3 (10-66.2)
IP-10/CXCL10	0.4559	0.6839	0.9992	1.012 (0.973, 1.042)	9.7 (5.1-18.6)	19.9 (6.2-40.9)	127.2 (83.8-205.5)	310.3 (97.2-464.7)
IL-9	0.483	0.6995	0.9992	1.012 (0.966, 1.039)	1.6 (0.5-4.8)	2.3 (1.8-11.7)	0.4 (0.2-1)	2.5 (0.3-4)
IL-4	0.0764	0.0764	0.3055	1.023 (0.991, 1.047)	2 (0-3.7)	4 (2.3-9.5)	0.6 (0.2-3.6)	4.9 (1.3-12.6)
MIP-1α	0.0591	0.0591	0.2364	1.021 (0.996, 1.042)	0.5 (0-10.3)	8.3 (0.1-49.2)	8.2 (0.6-19.9)	23.7 (3.2-40)
TGF-α	**0.0358**	**0.0358**	0.1433	1.028 (0.995, 1.053)	0.8 (0.1-2)	1 (0.3-4.1)	3.4 (1.3-7.1)	3.9 (1.5-13.2)
IL-18	0.1394	0.2928	0.5577	1.020 (0.990, 1.045)	13.1 (6.5-28.2)	12.7 (6.7-54.9)	108.5 (38.9-211)	218.1 (66.2-477.1)
IL-1α	**0.0239**	**0.0239**	0.0954	1.027 (0.999, 1.049)	0.2 (0-2.3)	2.6 (0.2-22)	3.1 (0.3-27.3)	50.4 (2.5-212.6)
IL-10	0.1339	0.2928	0.5354	1.020 (0.987, 1.045)	1.5 (0.1-4.3)	4.5 (0.8-19.8)	1.6 (0.3-4.3)	6 (2.1-10.2)
IL-17A	0.9498	0.9729	0.9992	1.001 (0.920, 1.034)	0.4 (0-2.1)	1.3 (0.6-2.7)	2 (0.6-9.1)	4.7 (2.3-13)
MDC	0.8532	0.8959	0.9992	0.996 (0.947, 1.033)	22.4 (14.2-35.6)	22.7 (14.5-36.1)	764.5 (495.4-1216.8)	954.4 (510.5-1782.7)
GM-CSF	0.1044	0.2739	0.4174	1.027 (0.983, 1.057)	0.9 (0.2-3.2)	1.2 (0.3-19.8)	6.3 (1.9-32.8)	42.8 (2.1-74.1)
PDGF-AA	0.6536	0.7999	0.9992	0.993 (0.954, 1.020)	22.7 (14-39.5)	21 (17.9-29.4)	1421.2 (1025.2-2138)	1324.8 (900.9-2412.9)
FGF-2	0.2576	0.4705	0.9992	1.017 (0.985, 1.046)	25.8 (8.4-39.1)	27.5 (11.1-39.8)	79.6 (57-100)	109.1 (88.7-147.2)
IL-5	**0.0472**	**0.0472**	0.1889	1.024 (0.996, 1.047)	0.7 (0.1-3.7)	4.2 (1.5-20.4)	0.2 (0-0.8)	1.7 (0.6-10)
Fractalkine	0.7676	0.8898	0.9992	1.005 (0.958, 1.030)	0 (0-1.3)	1.5 (0-11.7)	0.6 (0.6-19.5)	51.2 (0.6-303.4)
IFNa2	0.2185	0.4172	0.874	1.018 (0.977, 1.044)	0.1 (0-2.2)	1.4 (0-13.3)	0.6 (0.1-20)	16 (0.6-94.6)
sCD40L	0.6666	0.7999	0.9992	0.993 (0.958, 1.021)	20.9 (7.5-42.7)	9.9 (6.8-42.5)	1555.4 (431.9-3198.7)	960.6 (638.6-3254.8)
RANTES	0.3842	0.6454	0.9992	0.976 (0.908, 1.015)	11.6 (5.4-24.6)	11.1 (2.5-19.1)	377.3 (185.8-868.4)	409.8 (290.5-642)
IL-3	0.5044	0.7061	0.9992	1.012 (0.957, 1.042)	4.5 (1.2-9)	7.8 (4-13.9)	0.5 (0.4-0.6)	1.1 (0.6-1.5)
IL-12 p40	**0.0196**	**0.0196**	0.0782	1.031 (1.000, 1.056)	0.1 (0-1.9)	3.3 (0-14)	0.6 (0.6-17.7)	60 (0.6-165.1)
EGF	0.0606	0.0606	0.2425	1.023 (0.998, 1.047)	15.1 (3.2-31.7)	37 (6.9-69.2)	53.1 (13.8-133.9)	132.5 (40.6-303.9)
IL-13	**0.015**	**0.015**	0.0598	1.026 (1.002, 1.047)	0 (0-1)	1.6 (0-48.2)	0.7 (0.6-3.7)	15.5 (0.7-134.1)
Flt-3L	0.3787	0.6454	0.9992	1.014 (0.974, 1.042)	0 (0-10.1)	0 (0-9)	0.6 (0.1-30.1)	0.6 (0.1-67.9)
IL-1RA	**0.0253**	**0.0253**	0.1012	1.026 (1.000, 1.049)	1.7 (0-6.6)	4 (0.8-36.8)	13.5 (0.6-61.5)	82.2 (11.4-519.5)
GROa	0.402	0.6494	0.9992	0.967 (0.869, 1.019)	10.2 (6.7-17)	9.9 (6.4-12.7)	1080.3 (732.4-1567.8)	1040.1 (900.5-1579.7)
VEGF-A	0.7987	0.8898	0.9992	1.005 (0.960, 1.035)	9.8 (4-18.4)	14.5 (5.9-30.9)	120.9 (58-211)	184.3 (88.5-213.2)
IL-15	0.1337	0.2928	0.535	1.022 (0.986, 1.048)	3.1 (0.6-10.1)	7.2 (2.3-18.8)	1.7 (0.6-3.5)	7.2 (2.7-11.3)
IFNγ	0.5601	0.7589	0.9992	1.010 (0.962, 1.036)	0.8 (0-2.7)	1.7 (0.6-2.8)	2.7 (0.3-8.2)	4.9 (3.5-30.9)
IL-1β	0.5946	0.7805	0.9992	1.010 (0.957, 1.040)	0.1 (0-2.4)	1.3 (0.1-12.3)	0.6 (0.1-2)	2.2 (0.4-8.1)
IL-12 p70	0.2015	0.4031	0.8062	1.017 (0.984, 1.040)	0 (0-1.3)	0.1 (0-5.2)	0.6 (0.2-3.5)	2.3 (0.2-27.8)
MCP-3/CCL7	**0.0116***	**0.0116***	**0.0462***	**1.028 (1.004, 1.050)**	0 (0-3.8)	4.1 (0-53.7)	0.6 (0.6-23)	115.4 (0.6-361.7)
TNFβ	**0.0139**	**0.0139**	0.0554	1.027 (1.002, 1.048)	0 (0-0)	0.7 (0-42.9)	0.6 (0.6-0.6)	51.4 (0.6-729.7)
PDGF-BB	0.8263	0.8898	0.9992	0.997 (0.967, 1.022)	17.6 (11.2-61.5)	26.7 (18.7-47.9)	5326.3 (3621-14368.4)	5818.2 (4909.9-20256.2)
IL-2	0.0639	0.0639	0.2554	1.024 (0.991, 1.048)	0.1 (0-2.1)	0.6 (0-6.2)	0.4 (0-1.5)	2.5 (0-4.6)
MIP-1β	0.1124	0.2778	0.4498	1.024 (0.990, 1.052)	12.7 (5.2-23.2)	19.2 (7.9-26.6)	44.8 (18.6-70.3)	76.5 (31.4-121.2)

TET2 mutation vs. no mutation

Cytokine	Raw p-value	FDR-adjusted p-value	Bonferroni-adjusted p-value	OR (95% CI)	Median (IQR) No mutation^	Median (IQR) TET2^	Median (IQR) No mutation^^	Median (IQR) TET2^^
TNFα	0.1136	0.7473	0.4543	1.015 (0.996, 1.033)	22.3 (12.5-35.2)	26.1 (14.3-38.9)	17.5 (12.6-25.7)	20.8 (12.2-33.5)
IL-6	0.0833	0.0833	0.3331	1.017 (0.997, 1.034)	2.7 (0.5-6.5)	6.2 (1-12.1)	1.5 (0.3-3.6)	3.2 (0.7-6.4)
MCP-1/CCL2	0.5203	0.7473	0.8704	1.006 (0.988, 1.023)	35.4 (24.2-48.3)	37.5 (22.9-61.6)	434.9 (334.4-580.9)	494.8 (333.1-580.5)
Eotaxin1	0.2563	0.7473	0.8704	1.010 (0.992, 1.028)	30.2 (19.2-43.7)	33.5 (23.1-44.2)	118 (77.7-163.3)	129.6 (81-183.6)
IL-8	0.3345	0.7473	0.8704	1.009 (0.989, 1.025)	5.5 (2.3-13.6)	4.4 (2-15)	17.9 (10.3-35.7)	18 (9.3-50.5)
IL-7	0.2715	0.7473	0.8704	1.010 (0.992, 1.026)	11.6 (4.2-25.1)	17.9 (8.8-36.6)	2.8 (1.4-4.6)	3.6 (2.1-6.1)
G-CSF	0.1992	0.7473	0.7968	1.012 (0.992, 1.029)	1.1 (0.4-9.7)	1.3 (0.3-21.7)	3.2 (1.4-34.7)	3.3 (1.1-52.1)
IP-10/CXCL10	0.1583	0.7473	0.6332	1.014 (0.994, 1.032)	9.2 (4.7-17.5)	11.3 (5.9-28)	125.3 (79.9-202.3)	147.6 (84.3-310.3)
IL-9	0.6447	0.7657	0.8704	1.005 (0.982, 1.022)	1.6 (0.5-4.7)	2 (1.2-4.3)	0.4 (0.2-1)	0.3 (0.2-2.1)
IL-4	0.1547	0.7473	0.6188	1.013 (0.994, 1.030)	2 (0-3.7)	2.3 (0.8-3.7)	0.6 (0.2-3.6)	1.3 (0.3-4.9)
MIP-1α	0.252	0.7473	0.8704	1.009 (0.992, 1.024)	0.6 (0-8.1)	0.4 (0.1-8.5)	8.3 (0.6-20.8)	7.6 (1.7-19.9)
TGF-α	0.59	0.7508	0.8704	1.006 (0.978, 1.026)	0.8 (0.1-2)	0.8 (0.3-1.4)	3.5 (1.2-7.3)	2.6 (1.5-6)
IL-18	0.0868	0.0868	0.3471	1.014 (0.997, 1.030)	13.1 (6-28.2)	17.5 (7.8-40.7)	107.4 (38.8-205)	131 (54.8-271.5)
IL-1α	0.4598	0.7473	0.8704	1.008 (0.985, 1.025)	0.2 (0-2.3)	0.3 (0.1-1.6)	2.6 (0.1-27.7)	3.2 (0.9-41)
IL-10	0.4272	0.7473	0.8704	1.008 (0.985, 1.027)	1.4 (0.1-4.4)	1.6 (0.3-4.1)	1.6 (0.4-4.2)	2.1 (0.5-4.8)
IL-17A	0.4745	0.7473	0.8704	1.009 (0.980, 1.030)	0.3 (0-2)	0.8 (0.1-3.2)	1.8 (0.6-9.1)	2.6 (0.6-15.2)
MDC	0.2717	0.7473	0.8704	0.986 (0.959, 1.009)	22 (14.2-36)	22.7 (13.6-29)	784.1 (488.8-1218.3)	635.8 (493.1-1105.1)
GM-CSF	0.5202	0.7473	0.8704	1.008 (0.979, 1.029)	0.9 (0.3-3)	1.2 (0.2-7.1)	5.7 (1.9-29.6)	14.8 (2.1-50.7)
PDGF-AA	0.4572	0.7473	0.8704	1.006 (0.990, 1.020)	22.9 (14.2-38.8)	24 (16.8-44.2)	1408.8 (1039.3-2074.2)	1487.4 (960.9-2195)
FGF-2	0.2543	0.7473	0.8704	1.010 (0.992, 1.027)	26.9 (8.6-38.7)	34.4 (8.9-45.3)	79.2 (57.8-97.8)	88.7 (56.3-112.8)
IL-5	0.4318	0.7473	0.8704	1.008 (0.985, 1.026)	0.7 (0.1-4)	1.3 (0.1-5.6)	0.2 (0-0.8)	0.2 (0-1.3)
Fractalkine	0.3952	0.7473	0.8704	1.008 (0.987, 1.025)	0 (0-1.2)	0 (0-2.5)	0.6 (0.6-18.3)	0.8 (0.6-51.2)
IFNa2	0.7527	0.8347	0.8704	1.004 (0.974, 1.024)	0.1 (0-2)	0.1 (0-5.8)	0.6 (0.1-16)	1.3 (0.1-38)
sCD40L	0.7825	0.8427	0.8704	0.998 (0.981, 1.013)	20.8 (7.6-42.4)	16.5 (7.3-43.8)	1470.3 (421.5-3151.8)	1178.9 (432.7-3602.8)
RANTES	0.3615	0.7473	0.8704	0.991 (0.967, 1.008)	11.4 (5.4-22.3)	8.3 (2.8-17)	384.4 (188.8-893.3)	266 (165.7-582.3)
IL-3	0.6563	0.7657	0.8704	1.006 (0.976, 1.026)	4.5 (0.9-9)	6.1 (3.7-9.8)	0.5 (0.4-0.6)	0.5 (0.4-0.8)
IL-12 p40	0.5516	0.7473	0.8704	1.007 (0.981, 1.025)	0.1 (0-1.8)	0.3 (0-3.6)	0.6 (0.6-17.1)	4 (0.6-46.3)
EGF	0.4144	0.7473	0.8704	1.006 (0.991, 1.020)	16.4 (2.2-31.9)	16.7 (4.5-45.4)	55.2 (11.8-137.6)	83.4 (17.2-172.3)
IL-13	0.1788	0.7473	0.7154	1.010 (0.994, 1.024)	0 (0-2.3)	0 (0-2.1)	0.7 (0.6-5)	0.7 (0.6-8.2)
Flt-3L	0.8578	0.8704	0.8704	0.998 (0.974, 1.016)	0 (0-11.4)	0 (0-1.1)	0.6 (0.6-28.9)	0.6 (0.1-9.3)
IL-1RA	0.4239	0.7473	0.8704	1.007 (0.988, 1.022)	1.8 (0-7.2)	2.8 (0.1-6.5)	14.2 (0.6-73.1)	22 (1.2-113.9)
GROa	0.1917	0.7473	0.7667	0.976 (0.931, 1.007)	10.2 (6.5-17)	9.9 (7.6-13.1)	1056.8 (716-1493.7)	1040.1 (834.1-1422.5)
VEGF-A	0.8704	0.8704	0.8704	1.002 (0.977, 1.022)	10 (4.2-17.8)	10.5 (4.4-16.4)	121.4 (62.5-206)	157.3 (68.3-213.2)
IL-15	0.4727	0.7473	0.8704	1.007 (0.985, 1.024)	3.2 (0.6-10.1)	3 (0.2-18.6)	1.6 (0.8-3.4)	1.9 (0.3-4.9)
IFNγ	0.7552	0.8347	0.8704	1.004 (0.974, 1.024)	0.8 (0-2.9)	0.7 (0-2.4)	3.1 (0.3-8.3)	1.6 (0.3-8.1)
IL-1β	0.4148	0.7473	0.8704	1.008 (0.986, 1.025)	0 (0-1.9)	0.8 (0-9.8)	0.6 (0.1-1.9)	0.6 (0.1-2.7)
IL-12 p70	0.5827	0.7508	0.8704	1.006 (0.982, 1.023)	0 (0-1.1)	0 (0-1.3)	0.6 (0.2-3.5)	0.3 (0.2-8.5)
MCP-3/CCL7	0.5427	0.7473	0.8704	1.005 (0.987, 1.020)	0 (0-4.9)	0 (0-4.4)	0.6 (0.6-37.2)	0.6 (0.6-44.9)
TNFβ	0.524	0.7473	0.8704	1.006 (0.986, 1.021)	0 (0-0)	0 (0-0.3)	0.6 (0.6-2.3)	0.6 (0.6-22.4)
PDGF-BB	0.8281	0.8695	0.8704	0.999 (0.984, 1.011)	17.6 (11.3-61.5)	17 (10.9-61.5)	5339.3 (3657.5-14915.5)	5031.3 (3549.5-21217.9)
IL-2	0.3862	0.7473	0.8704	1.009 (0.986, 1.026)	0.1 (0-2.1)	0 (0-2.8)	0.5 (0-1.9)	0 (0-3.6)
MIP-1β	0.6325	0.7657	0.8704	1.005 (0.984, 1.022)	12.9 (5.5-23.3)	14.7 (2-28.9)	44.3 (20-71.2)	52.5 (13.5-76.5)

DNMT3A mutation vs. no mutation

Cytokine	Raw p-value	FDR-adjusted p-value	Bonferroni-adjusted p-value	OR (95% CI)	Median (IQR) No mutation^	Median (IQR) DNMT3A^	Median (IQR) No mutation^^	Median (IQR) DNMT3A^^
TNFα	**0.0285**	**0.0473**	0.1141	1.020 (1.002, 1.038)	22.3 (12.5-35.2)	31.2 (20.3-50.9)	17.5 (12.6-25.7)	20.2 (16.2-32.3)
IL-6	**0.0027***	**0.0108***	**0.0108***	**1.026 (1.009, 1.043)**	2.7 (0.5-6.5)	3.4 (0.8-31.7)	1.5 (0.3-3.6)	1.7 (0.5-8.7)
MCP-1/CCL2	0.2552	0.5786	0.9959	1.010 (0.992, 1.029)	35.4 (24.2-48.3)	37.4 (22.7-61.9)	434.9 (334.4-580.9)	446.1 (325-678.3)
Eotaxin1	0.1982	0.5786	0.793	1.013 (0.993, 1.032)	30.2 (19.2-43.7)	35.9 (23.3-53)	118 (77.7-163.3)	157.5 (99.3-202.4)
IL-8	0.0619	0.0619	0.2477	1.015 (0.998, 1.031)	5.5 (2.3-13.6)	8.2 (5.8-16.7)	17.9 (10.3-35.7)	24.1 (18-38.8)
IL-7	0.272	0.5786	0.9959	1.010 (0.991, 1.026)	11.6 (4.2-25.1)	17.5 (3.2-29.6)	2.8 (1.4-4.6)	2.6 (1.4-7.2)
G-CSF	0.1949	0.5786	0.7794	1.012 (0.992, 1.030)	1.1 (0.4-9.7)	1.5 (0.4-19.9)	3.2 (1.4-34.7)	3.8 (1-34.7)
IP-10/CXCL10	0.2538	0.5786	0.9959	1.012 (0.990, 1.031)	9.2 (4.7-17.5)	10.5 (7.1-25.3)	125.3 (79.9-202.3)	143.5 (96.9-238)
IL-9	0.4286	0.6923	0.9959	1.008 (0.986, 1.025)	1.6 (0.5-4.7)	1.6 (0.5-5.6)	0.4 (0.2-1)	0.4 (0.2-2.1)
IL-4	0.0989	0.0989	0.3955	1.016 (0.996, 1.034)	2 (0-3.7)	2.3 (0.3-3.7)	0.6 (0.2-3.6)	1 (0.4-4.8)
MIP-1α	**0.0355**	**0.0473**	0.142	1.016 (1.000, 1.030)	0.6 (0-8.1)	0.4 (0-22.1)	8.3 (0.6-20.8)	7.6 (0.6-20.8)
TGF-α	0.2213	0.5786	0.8851	1.013 (0.990, 1.032)	0.8 (0.1-2)	1 (0.3-4.2)	3.5 (1.2-7.3)	3.7 (1.4-11)
IL-18	0.9626	0.9861	0.9959	1.000 (0.979, 1.019)	13.1 (6-28.2)	9.2 (6.1-23.5)	107.4 (38.8-205)	133.9 (32.1-228.2)
IL-1α	0.1738	0.5786	0.6951	1.012 (0.993, 1.028)	0.2 (0-2.3)	0.2 (0-3.9)	2.6 (0.1-27.7)	1.2 (0.1-42.1)
IL-10	0.2604	0.5786	0.9959	1.012 (0.989, 1.030)	1.4 (0.1-4.4)	1.6 (0-3.9)	1.6 (0.4-4.2)	1.3 (0-4.6)
IL-17A	0.1865	0.5786	0.7458	1.014 (0.992, 1.033)	0.3 (0-2)	0.5 (0-4.8)	1.8 (0.6-9.1)	2.6 (0.5-21.7)
MDC	0.1546	0.5786	0.6183	1.014 (0.994, 1.033)	22 (14.2-36)	27.6 (16.1-41.1)	784.1 (488.8-1218.3)	665.5 (505.1-1664.4)
GM-CSF	0.3438	0.6016	0.9959	1.011 (0.986, 1.029)	0.9 (0.3-3)	0.4 (0.2-4.4)	5.7 (1.9-29.6)	4.1 (1.7-8.9)
PDGF-AA	0.9959	0.9959	0.9959	1.000 (0.982, 1.016)	22.9 (14.2-38.8)	16 (10.6-31.4)	1408.8 (1039.3-2074.2)	1184.1 (794.9-2443.5)
FGF-2	0.7554	0.9064	0.9959	1.003 (0.983, 1.021)	26.9 (8.6-38.7)	23.7 (9.4-39.8)	79.2 (57.8-97.8)	75 (49.6-101.8)
IL-5	0.1209	0.5786	0.4834	1.014 (0.995, 1.031)	0.7 (0.1-4)	0.2 (0.1-5.6)	0.2 (0-0.8)	0.1 (0-0.9)
Fractalkine	0.2923	0.5846	0.9959	1.010 (0.989, 1.027)	0 (0-1.2)	0 (0-4.1)	0.6 (0.6-18.3)	0.6 (0.6-102.7)
IFNa2	0.2579	0.5786	0.9959	1.011 (0.990, 1.028)	0.1 (0-2)	0 (0-2)	0.6 (0.1-16)	0.6 (0.1-13.4)
sCD40L	0.6235	0.8735	0.9959	0.996 (0.978, 1.012)	20.8 (7.6-42.4)	18.4 (6.6-38.3)	1470.3 (421.5-3151.8)	1567.4 (394.8-3151.5)
RANTES	0.6674	0.8759	0.9959	1.003 (0.986, 1.018)	11.4 (5.4-22.3)	13.5 (8-26.2)	384.4 (188.8-893.3)	556.8 (263.4-989.7)
IL-3	0.9177	0.9635	0.9959	1.001 (0.964, 1.023)	4.5 (0.9-9)	4.1 (1.8-8.2)	0.5 (0.4-0.6)	0.5 (0.4-0.6)
IL-12 p40	0.4232	0.6923	0.9959	1.009 (0.984, 1.027)	0.1 (0-1.8)	0 (0-0.2)	0.6 (0.6-17.1)	0.6 (0.3-4)
EGF	0.312	0.5956	0.9959	0.990 (0.969, 1.008)	16.4 (2.2-31.9)	7.6 (0.4-26.8)	55.2 (11.8-137.6)	25.5 (2.3-85.6)
IL-13	0.8891	0.9635	0.9959	1.001 (0.978, 1.018)	0 (0-2.3)	0 (0-0.1)	0.7 (0.6-5)	0.7 (0.6-0.7)
Flt-3L	0.2755	0.5786	0.9959	1.010 (0.991, 1.026)	0 (0-11.4)	0.4 (0-23.1)	0.6 (0.6-28.9)	1 (0.1-67.9)
IL-1RA	0.7181	0.8871	0.9959	1.003 (0.982, 1.020)	1.8 (0-7.2)	0.3 (0-3.1)	14.2 (0.6-73.1)	3.8 (0.6-46.5)
GROa	0.121	0.5786	0.4838	1.014 (0.995, 1.031)	10.2 (6.5-17)	9.1 (6.8-21.4)	1056.8 (716-1493.7)	1203.2 (890.9-1915.1)
VEGF-A	0.6242	0.8735	0.9959	0.993 (0.963, 1.017)	10 (4.2-17.8)	11.4 (0.3-18.9)	121.4 (62.5-206)	106.7 (3.2-234.5)
IL-15	0.8602	0.9635	0.9959	0.998 (0.967, 1.018)	3.2 (0.6-10.1)	3.2 (0.6-7.4)	1.6 (0.8-3.4)	1.7 (0.6-3.4)
IFNγ	0.1678	0.5786	0.6713	1.013 (0.993, 1.030)	0.8 (0-2.9)	1 (0-2.5)	3.1 (0.3-8.3)	3.4 (0.2-7.6)
IL-1β	0.6447	0.8735	0.9959	0.993 (0.949, 1.017)	0 (0-1.9)	0 (0-3.1)	0.6 (0.1-1.9)	0.4 (0.1-2.1)
IL-12 p70	0.3436	0.6016	0.9959	1.009 (0.988, 1.026)	0 (0-1.1)	0 (0-0.1)	0.6 (0.2-3.5)	0.6 (0.2-1.4)
MCP-3/CCL7	0.9142	0.9635	0.9959	1.001 (0.980, 1.017)	0 (0-4.9)	0 (0-0)	0.6 (0.6-37.2)	0.6 (0.6-0.6)
TNFβ	0.7135	0.8871	0.9959	1.003 (0.982, 1.020)	0 (0-0)	0 (0-0)	0.6 (0.6-2.3)	0.6 (0.6-0.6)
PDGF-BB	0.8347	0.9635	0.9959	0.998 (0.984, 1.012)	17.6 (11.3-61.5)	22.9 (11.9-39.3)	5339.3 (3657.5-14915.5)	5511.3 (3879-11694.7)
IL-2	0.6132	0.8735	0.9959	1.006 (0.979, 1.024)	0.1 (0-2.1)	0 (0-1.6)	0.5 (0-1.9)	0 (0-0.6)
MIP-1β	0.6166	0.8735	0.9959	0.994 (0.967, 1.015)	12.9 (5.5-23.3)	9.8 (0.4-24.2)	44.3 (20-71.2)	38.3 (1.5-66.5)

^Min-max (0-100) normalized cytokine value group medians (to reduce batch effects)
^^pg/mL cytokine level group medians (not normalized)