ID	Gene	Type	VAF	Substitution	Mutational Detail	Chromosome	StartPosition	CoverageTotal	CoverageRef	CoverageAlt	Variant Assessment
1	DNMT3A	Missense	6%	T>C	c.1031T>C; p.L344P	2	25470011	839	792	47	COSMIC ID COSV53037012
2	DNMT3A	Missense	15%	C>T	c.2206C>T; p.R736C	2	25463287	924	781	142	COSMIC ID COSV53038112
3	DNMT3A	Nonsense	6%	G>A	c.915G>A; p.W305*	2	25470559	1259	1183	76	COSMIC ID COSV53067969
4	NRAS	Missense	3%	G>A	c.35G>A; p.G12D	1	115258747	217	210	7	COSMIC ID COSV54736383
	SRSF2	Missense	4%	C>A	c.284C>A; p.P95H	17	74732959	171	165	6	COSMIC ID COSV57969816
5	CHEK2	Frameshift	34%		c.1100delC; p.T367Mfs*15	22	29091857	1475	971	504	This frameshift alteration has been previously reported as variant and is expected to be pathogenic. Clinvar ID 128042, GnomAD 0.0026
6	DNMT3A	Frameshift	11%		c.2612delC; p.P871Qfs*10	2	25457274	1038	925	113	This frameshift alteration has not been previously reported to our know ledge, but it is expected to be pathogenic.
7	SRSF2	Missense	3%	C>A	c.284C>A; p.P95H	17	74732959	197	191	6	COSMIC ID COSV57969816
8	MSH6	Frameshift	11%		c.3261delC; p.F1088Sfs*2	2	48030640	197	176	21	COSMIC ID COSV52273658
9	MYD88	Missense	14%	T>C	c.794T>C; p.L265P	3	38182641	621	534	87	COSMIC ID COSM166298
10	U2AF1	Missense	8%	A>C	c.470A>C; p.Q157P	21	44514777	709	655	53	COSMIC ID COSV52341120
11	MDM4	Missense	11%	T>C	c.1099T>C; p.S367P	1	204518436	955	851	103	This missense alteration has not been previously reported to our know ledge; how ever it is expected to be pathogenic
12	ATM	Frameshift	38%		c.5712dupA; p.S1905Ifs*25	11	108178655	686	424	262	COSMIC ID COSV99589337
13	STAT3	Inframe insertion	30%		c.1969_1971dupTAT; p.Y657dup	17	40474429	1343	939	404	This missense alteration has not been previously reported to our know ledge; how ever it is expected to be pathogenic (activating mutant) based on PMID: 21690253
14	BCOR	Missense	6%	C>A	c.2870C>A; p.P957Q	X	39931729	143	135	8	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
	BCOR	Missense	7%	G>T	c.980G>T; p.G327V	X	39933619	101	94	7	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
	MEF2B	Missense	5%	C>A	c.874C>A; p.Q292K	19	19257089	215	204	11	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
15	NRAS	Missense	4%	G>T	c.38G>T; p.G13V	1	115258744	1050	1013	37	COSMIC ID COSV54736480
16	DNMT3A	Missense	9%	C>T	c.2695C>T; p.R899C	2	25457192	954	873	81	COSMIC ID COSV53070898
17	IDH2	Missense	9%	G>A	c.419G>A; p.R140Q	15	90631934	839	763	76	COSMIC ID COSV57468751
	SRSF2	Missense	8%	C>A	c.284C>A; p.P95H	17	74732959	702	644	58	COSMIC ID COSV57969816
18	SF3B1	Insertion	28%		c.667-4_667-3insT; splice region	2	198274734	1138	820	318	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain. Freq < 0.0000 in ALFA
19	ATM	Missense	12%	G>T	c.9152G>T; p.G3051V	11	108236216	751	660	91	COSMIC ID COSV53735826
20	TERT	SNP	10%	C>T	c.-146C>T;	5	1295250	292	264	28	This promoter alteration has been previously reported (PMID: 26143636), and is expected to be pathogenic.
21	CBL	Missense	32%	G>A	c.1151G>A; p.C384Y	11	119148931	1038	706	332	COSMIC ID COSV50633156
22	DNMT3A	SNP	9%	G>A	c.2173+1G>A; splice-site	2	25463508	956	870	85	This splice-site alteration is expected to be pathogenic since it affects the invariant splice donor sequence; COSMIC ID COSV53056806
23	CREBBP	Nonsense	5%	A>T	c.4513A>T; p.K1505*	16	3786698	877	830	47	This nonsense alteration has not been previously reported to our know ledge, but is expected to be pathogenic.
24	EGR1	Missense	13%	G>A	c.1339G>A; p.A447T	5	137803477	792	691	101	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
25	ATRX	Missense	8%	A>C	c.3956A>C; p.Q1319P	x	76919035	406	372	34	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
26	ETV6	Frameshift	17%		c.1277_1278insTTAT; p.M427Yfs*19	12	12043896	616	512	104	This frameshift alteration has not been previously reported to our know ledge, but is expected to be pathogenic.
	SF3B1	Missense	14%	A>G	c.2098A>G; p.K700E	2	198266834	985	848	137	COSMIC ID COSV59205318
	TET2	Frameshift	13%		c.2454_2455insA; p.Y819Ifs*2	4	106157553	867	756	111	This frameshift alteration has not been previously reported to our know ledge, but is expected to be pathogenic.
27	TET2	Missense	7%	C>A	c.4240C>A; p.Q1414K	4	106193778	1071	994	77	COSMIC ID COSV54421241
28	TP53	Missense	33%	T>C	c.584T>C; p.I195T	17	7578265	886	597	289	COSMIC ID COSV52664264
29	DNMT3A	Frameshift	12%		c.2237delG; p.G746Efs*33	2	25463255	1097	965	132	This frameshift alteration has not been previously reported to our know ledge, but is expected to be pathogenic.
30	MSH6	Frameshift	14%		c.3261delC; p.F1088Sfs*2	2	48030640	225	193	32	COSMIC IS COSV52273658
31	SETBP1	Missense	10%	C>G	c.2491C>G; p.P831A	18	42531796	1190	1071	119	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
32	TET2	Missense	7%	A>G	c.3797A>G; p.N1266S	4	106164929	852	792	60	This nonsense alteration has not been previously reported to our know ledge, but is expected to be pathogenic.
33	DNMT3A	Frameshift	16%		c.2223delG; p.R742Gfs*37	2	25463270	1367	1143	224	This frameshift alteration has not been previously reported to our know ledge, but is expected to be pathogenic.
34	BRAF	Missense	6%	G>A	c.1040G>A; p.R347Q	7	140494208	1097	1028	69	COSMIC ID COSM1315830
35	DNMT3A	Nonsense	8%	G>A	c.2579G>A; p.W860*	2	25458594	893	825	68	COSMIC ID COSV53036852
36	DNMT3A	SNP	8%	G>A	c.1429+1G>A	2	25469028	1140	1046	94	COSMIC ID COSV53047449
37	SF3B1	Missense	16%	G>A	c.2219G>A; p.G740E	2	198266713	1097	923	174	COSMIC ID COSV59205460
38	TP53	Missense	11%	G>A	c.824G>A; p.C275Y	17	7577114	1408	1251	157	COSMIC ID COSV52661919
39	DNMT3A	Nonsense	10%	C>T	c.1792C>T; p.R598*	2	25467083	779	704	75	COSMIC ID COSV53039812
40	PDGFRB	Missense	21%	G>A	c.1990G>A; p.V664M	5	149503846	607	482	125	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
41	DNMT3A	Frameshift	12%		c.957_962delCCGAGCinsAGAGAGA G; p.S319Rfs*27	2	25470511	1424	1258	166	The frameshift alteration has not been previously reported to our know ledge, but is expected to be pathogenic
42	DNMT3A	SNP	39%	G>A	c.1667+1G>A	2	25467408	615	377	238	COSMIC ID COSV53043167
	TET2	Frameshift	38%		c.285delA; p.K95Nfs*18	4	106255380	1024	631	393	COSMIC ID COSV54407645
43	TET2	SNP	6%	A>G	c.3410-2A>G;	4	106162494	465	436	29	COSMIC ID COSV99485035
44	DNMT3A	Missense	21%	C>G	c.2671C>G; p.R891G	2	25457216	1475	1171	303	This missense alteration has not been previously reported to our know ledge, but is expected to be pathogenic
45	TET2	Nonsense	16%	C>T	c.4954C>T; p.Q1652*	4	106196621	1143	964	179	COSMIC ID COSV54418649
46	DNMT3A	SNP	25%	A>G	c.1937-2A>G	2	25464578	807	609	198	This splice-site alteration has not been previously reported to our know ledge, but is expected to be pathogenic since it affects the invariant acceptor splice-site.
47	DNMT3A	Missense	10%	A>C	c.1894A>C; p.K632Q	2	25466809	686	619	67	This missense alteration has not been previously reported to our know ledge, but is expected to be pathogenic
48	MDM4	Missense	5%	C>A	c.1424C>A; p.P475H	1	204518761	252	239	13	This missense alteration has not been previously reported to our know ledge, and its clinical significance is uncertain.
	MTOR	SNP	5%	C>A	c.7367-5C>A	1	11169791	190	179	11	This splice-region alteration has not been previously reported to our know ledge, and its clinical significance is uncertain as it does not affect the invariant acceptor splice-site.
	TET2	Missense	5%	G>T	c.3938G>T; p.G1313V	4	106180910	180	170	10	This missense alteration has not been previously reported to our know ledge, but is expected to be pathogenic

Supplemental Table 1: Nonsynonymous alterations seen in WTC-exposed first responders: A total of 57 mutations were seen in 48 subjects.

ID	Gene	Type	VAF	Amino Acid Change	Nucleoitide Change	Chromosome	StartPosition	CoverageTotal	CoverageRef	CoverageAlt	Variant Assessment
1	DNMT3A	Frameshift	12.2%	p.W860Nfs*22	NM_022552.4:c 2577_2578insAA	2	25458595	869	763	106	This frameshift alteration has not been previously reported to our know ledge, but it is expected to be pathogenic.
2	TET2	Stop gained	18.5%	p.L862*	NM_001127208.2:c. 2585T>A	4	106157684	969	789	180	This frameshift alteration has not been previously reported to our know ledge, but it is expected to be pathogenic.
3	ASXL1	Stop gained	5.4%	p.E865*	NM_015338.6:c. 2593G>T	20	31023108	1307	1237	70	This frameshift alteration has not been previously reported to our know ledge, but it is expected to be pathogenic.
4	TERT	Promoter	9.0%	promotor c.-124C>T	NM_198253.3:c.-124C>T	5	1295228	343	312	31	MedGen UID: 1389413
5	TP53	Missense	8.40%	p.R248W	NM_000546.5:c. 742C>T	17	7577539	869	769	73	COSMIC ID COSV52662035
	FGFR2	Missense	6.9%	G552R	NM-000141.4:c. 1654G>A	10	123258027	538	500	38	This missense variant, located in the protein kinase domain, has not been previously reported or functionally characterized in the scientific literature to our knowledge. Therefore, its clinical significance is uncertain.
6	TET2	Stop gained	29%	p.W1847*	NM_001127208.2:c. 5541G>A	4	106197208	1304	926	378	COSMIC ID COSV54399228
	KMT2D	Frameshift	32%	p.E4438Gfs*45	NM_003482.3:c. 13313_13323del	12	49425164	1362	926	436	This missense alteration has not been previously reported or functionally characterized in the scientific literature to our knowledge. Therefore, its clinical significance is uncertain
7	TET2	Missense	8.8%	p.H1881R	NM_001127208.2:c. 5642A>G	4	106197309	1019	929	90	COSMIC ID COSV54397947
8	STAT3	Missense	21.9%	p.Y640F	NM_139276.2:c.1919A>T	17	40474482	914	714	200	COSMIC ID COSV52882807
9	IDH2	Missense	1.4%	p.R140Q	NM_002168.3:c. 419G>A	15	90631934	651	451	10	COSMIC ID COSV57468751
	DNMT3A	Missense	15.2%	p.G654V	NM_022552.4:c. 1961G>T	2	25464552	929	787	142	This missense alteration has not been previously reported or functionally characterized in the scientific literature to our knowledge. Therefore, its clinical significance is uncertain.
10	PPM1D	Frameshift	16.1%	p.F534*	NM_003620.4:c. 1599_1611del	17	58740692	1273	1068	205	This missense alteration has not been previously reported or functionally characterized in the scientific literature to our knowledge. Therefore, its clinical significance is uncertain
11	TP53	Missense	9.3%	p.Y234C	NM_000546.5:c. 701A>G	17	7577580	503	456	47	COSMIC ID COSV52661201
12	PPM1D	Stop gained	6.30%	p.R552*	NM_003620.4:c. 1654C>T	17	58740749	1178	1104	74	COSMIC ID COSV59954404
13	IDH1	Missense	1.0%	p.R132H*	NM_005896.3:c. 395G>A	2	209113112	668	661	7	COSMIC ID COSV61615239
14	ASXL1	Frameshift	19.1	p.G646Wfs*12	NM_015338.6:c.1934dup	20	31022441	1240	1003	237	COSMIC ID COSV60102155
	U2AF1	Missense	25.40%	p.Q157P	NM_006758.2:c.470A>C	21	44514777	7221	538	183	COSMIC ID COSV52341120
15	DNMT3A	Missense	9.0%	G685R	NM_022552.4:c 2053G>A	2	25464460	781	711	70	COSMIC ID COSV53038183
16	PTEN	Missense	7.00%	P354L	NM_000314.8:c. 1061C>T	10	89725078	781	711	55	COSMIC ID COSV64294840
17	IDH2	Missense	11.0%	p.R140Q	NM_002168.3:c. 419G>A	15	90631934	839	736	76	COSMIC ID COSV57468751

Supplemental Table 2: Nonsynonymous alterations seen in non-WTC exposed firefighter controls responders: A total of 19 mutations were seen in 16 subjects.

Supplemental Table 3: Blood counts in WTC-exposed first responders: Presence of mutations does not appear to correlate with cytopenias as both groups have no significant cytopenias. 481 cases with available blood counts were included in analysis.

	Mutation Negative Cohort Median (Q1, Q3) (N=433)	**Mutation Positive Cohort** Median (Q1, Q3) (N=48)
Hemoglobin (g/dL)	14.8 (14.2, 15.4)	14.7 (13.8, 15.6)
Platelets (k/uL)	218.0 (175.5, 256.0)	221.5 (170.5, 259.0)
WBC (k/uL)	6.1 (5.0, 7.6)	6.8 (5.4, 7.9)
Neutrophil Count (k/uL)	3718.0 (2952.0, 4802.0)	4246.0 (3157.5, 5462.5)

n=1 participant without a mutation were missing platelet counts

Supplemental Table 4: Antibodies used for FACS analysis.

Antibody-Fluorophore	Clone	Final Dilution
Gr1 - PE	RB6-8C5	1:100
CD4 - PE-Cy5	GK1.5	1:100
CD8α - PE-Cy5	53-6.7	1:100
B220 - PE-Cy5	RA3-6B2	1:100
CD19 - PE-Cy5	eBio1D3	1:100
Ter119 PE-Cy5	TER-119	1:100
Sca1 – BV421 (PB)	D7	1:100
c-kit - APC	2B8	1:100
CD34 - FITC	RAM34	1:100
FcγR II/III (CD16/32) – PE-Cy7	93	1:100