Integrated genetic and clinical prognostic factors for aggressive adult T-cell leukemia/lymphoma

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Supplemental Information

Summary of Supplemental Information

Supplemental Methods explain our methods regarding the diagnostic criteria, collection of clinical data and tumor DNA, targeted capture sequencing, detailed statistical methods, statistical software, and elastic-net penalized Cox regression.
Supplemental Table 1 lists mutated genes analyzed in this study.
Supplemental Table 2 lists the mutations detected in the entire study cohort.
Supplemental Table 3 lists the associations between clinical variables or risk factors and gene mutations.
Supplemental Table 4 lists the results of the elastic-net penalized Cox regression.
Supplemental Figure 1 shows patient flow for the training and validation cohorts.
Supplemental Figure 2 shows overall survival of the training cohort.
Supplemental Figure 3 shows mutation frequencies of the training and validation cohorts.
Supplemental Figure 4 shows targeted mutational landscapes of the training and validation cohorts.
Supplemental Figure 5 shows the frequencies of mutated genes by mutation status for the 13 most commonly mutated genes.
Supplemental Figure 6 shows the positions and frequencies of mutations in representative genes.
Supplemental Figure 7 shows the results of univariate Cox analysis and survival curves for significant genes.
Supplemental Figure 8 shows co-occurrence relationships between mutated genes.
Supplemental Figure 9 shows survival curves for different mutational combinations.
Supplemental Figure 10 shows a comparison of risk categories determined by the m7-ATLPI considering mutations only vs. mutations plus copy number alterations (CNAs).
Supplemental Figure 11 shows the prognostic value of the m7-ATLPI for overall survival in the entire study cohort.
Supplemental Figure 12 shows the prognostic value of the m7-ATLPI in patients who received immunochemotherapy or allo-HSCT.
Supplemental Figure 13 shows survival curves according to *CCR4* mutational status in patients treated with immunochemotherapy.
Supplemental Reference

Supplemental Methods

Diagnostic criteria

Diagnostic criteria of patients with aggressive ATL were based on the World Health Organization classification, and patients were classified into acute, lymphoma, and unfavorable chronic subtypes according to the International Consensus Meeting proposal[1,2]. HTLV-1 infection was documented in all patients.

Collection of clinical data

Detailed clinical data were collected by case report form, and included the following. Data at diagnosis: date of diagnosis, age at diagnosis, sex, Eastern Cooperative Oncology Group performance status, complete blood count, lactate dehydrogenase level, blood urea nitrogen level, corrected calcium level, C-reactive protein level, albumin level, soluble interleukin-2 receptor level, and the Ann Arbor staging classification. Treatment-related data: treatment regimens, date of allogeneic hematopoietic stem-cell transplantation (allo-HSCT), and date of mogamulizumab administration. Survival data: date of last follow-up or death.

Collection of tumor DNA

Samples were collected according to approved protocols. Fresh samples were collected from patients after written informed consent was obtained. Frozen and formalin-fixed paraffin-embedded (FFPE) samples were collected from patients who had provided informed consent in the form of an opt-out on the website. Genomic DNA was isolated from peripheral blood or tumor ATL cells using the QIAamp DNA Mini Kit (Qiagen), or from 3-5 sections of 10-20 μm slices of formalin-fixed paraffin-embedded tumor biopsies using the QIAamp DNA FFPE Tissue Kit (Qiagen).

Targeted capture sequencing

Mutation analysis of blood or tissue samples obtained before treatment was performed by targeted sequencing, as previously reported[4]. Targeted capture was performed using a SureSelect Custom Kit (Agilent Technologies), which was designed to capture 50 recurrently mutated genes (Supplemental Table 1). Somatic mutations were called by Genomon pipeline version 2.6.2 (https://github.com/Genomon-Project/), and filtered by removing (i) synonymous single nucleotide variants (SNVs); (ii) known variants listed in the SNP databases unless they were identified ≥ 10 times in COSMIC database version 70; (iii) variants only present in unidirectional reads; (iv) variants occurring within repetitive genomic regions; and (v) variants with supporting reads < 4 in tumors. Unless identical mutations were (i) detected in other ATL cases or (ii) counted ≥ 10 times in COSMIC database version 70, candidate mutations were further filtered by excluding (i) mutations with allele frequency < 0.1 and (ii) all missense SNVs with allele frequency of 0.4–0.6 or 0.9–1. Finally, mapping errors were removed by visual inspection with the Integrative Genomics Viewer. The mean sequencing depth was 1,026 x.

Detailed statistical methods

Comparisons of patient characteristics between groups were carried out with the Mann–Whitney U test and Fisher's exact tests for continuous and categorical variables, respectively. The Kaplan-Meier method was used to estimate OS, and the log-rank test was used to assess differences in OS between patient groups. The effects of risk factors on overall survival (OS) were evaluated by Cox proportional hazards regression modeling with or without adjustment for clinical factors. For the training set, we performed univariable and multivariable analyses for genes mutated in 15% or more of the individuals in the cohort; that is, these genes were studied for their correlation with the ATL-PI and its individual components, as well as other clinical parameters and outcomes. The Bonferroni–Holm procedure was used to adjust for multiple testing. Correlation matrix analysis was performed to explore the statistically co-occurring combinations of genetic variants, and the FDR procedure was used to adjust for multiple testing. The aim of this study was to generate a clinicogenetic risk model to predict the prognosis of first-line intensive cytotoxic chemotherapy. Therefore, when developing the clinicogenetic risk models, patients who received mogamulizumab therapy or underwent allo-HSCT were censored on the day of mogamulizumab administration or allo-HSCT, respectively, to reduce the impact of these therapies on OS. To increase model stability, we considered clinical variables and the 13 genes with a mutation frequency of 15% or higher, irrespective of the results of univariable testing. For feature selection, we used elastic-net regression with a Cox proportional hazards model[18]. In the final model, a prognostic score was calculated as the sum of predictor values weighted by the elastic net coefficients, then the ranked prognostic scores of approximately the top and bottom 20th percentiles were set as cutoffs to divide each cohort into low-, intermediate-, and high-risk groups. This elastic-net model was trained only on the training set, and was then applied to the independent validation set to obtain predictions. The predictions were evaluated using the hazard ratio (HR), log-rank test, C-index, and time-dependent receiver operating characteristic (ROC) metrics. P values were calculated using two-sided tests, where $p < 0.05$ was considered statistically significant.

Statistical software

Statistical analyses were performed using R (version 4.1.2) and the R packages ggplot2 (version 3.3.5), corrplot (version 0.91), survival (version 3.2-13), glmnet (version 4.1-2), survcomp (version 1.40.0), and timeROC (version 0.4).

Elastic-net penalized Cox regression

The elastic net is a regularized regression framework that is a linear combination of the L1 (Lasso regression) and L2 (Ridge regression) penalties[5]. The performance of the model was rigorously evaluated using 10-fold cross-validation that was repeated 100 times. The optimal parameters that minimized the mean squared error were selected, then the elastic-net coefficients were determined.

Supplemental Tables

Supplemental Table 1. Mutated genes analyzed in this study.

PLCG1	*PRKCB*	*CCR4*	*CARD11*	*STAT3*	*TP53*	*VAV1*	*TBL1XR1*	*NOTCH1*	*GATA3*
IRF4	*FAS*	*CCR7*	*POT1*	*IRF2BP2*	*TET2*	*RHOA*	*HLA-B*	*HNRNPA2B1*	*EP300*
CD58	*GPR183*	*CSNK1A1*	*CSNK2B*	*CBLB*	*FYN*	*B2M*	*SETD2*	*ZNF638*	*ATXN1*
CSNK2A1	*ZEB1*	*CD28*	*KDM6A*	*PIK3CD*	*S1PR1*	*ZFP36L2*	*JAK3*	*DNMT3A*	*PTPRC*
YTHDF2	*PDE7B*	*CDKN2A*	*NOXA1*	*RELA*	*IDH2*	*TNFAIP3*	*NFKBIA*	*KMO*	*IKBKB*

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
KMO	nonsynonymous SNV	NM_003679	c.G1343A	p.R448Q	1	241755337	241755337	G	A	588	0.364	Training	Haem_ATL_1
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	752	0.532	Training	Haem_ATL_1
CCR4	frameshift deletion	NM_005508	c.998_1020del	p.G333fs	3	32995912	32995934	GGCTCCTCCAAATTTACTCTGCT	-	1342	0.124	Training	Haem_ATL_2
TBL1XR1	nonsynonymous SNV	NM_024665	c.C1168T	p.H390Y	3	176752068	176752068	G	A	592	0.421	Training	Haem_ATL_2
CARD11	nonsynonymous SNV	NM_032415	c.C1853G	p.S618C	7	2963954	2963954	G	C	798	0.264	Training	Haem_ATL_2
RELA	nonsynonymous SNV	NM_021975	c.G115C	p.E39Q	11	65429479	65429479	C	G	1064	0.282	Training	Haem_ATL_2
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1010	0.421	Training	Haem_ATL_2
TP53	nonframeshift deletion	NM_000546	c.754_762del	p.252_254del	17	7577519	7577527	GATGGTGAG	-	663	0.259	Training	Haem_ATL_2
STAT3	nonsynonymous SNV	NM_003150	c.C1842G	p.S614R	17	40475068	40475068	G	C	866	0.042	Training	Haem_ATL_2
VAV1	nonsynonymous SNV	NM_005428	c.C2368T	p.R790C	19	6853993	6853993	C	T	973	0.049	Training	Haem_ATL_2
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	1122	0.029	Training	Haem_ATL_2
TET2	nonsynonymous SNV	NM_001127208	c.T3686G	p.L1229R	4	106164818	106164818	T	G	286	0.378	Training	Haem_ATL_3
IKBKB	nonsynonymous SNV	NM_001556	c.G607A	p.V203I	8	42166458	42166458	G	A	312	0.423	Training	Haem_ATL_3
NOTCH1	stopgain	NM_017617	c.C7318T	p.Q2440X	9	139390873	139390873	G	A	291	0.172	Training	Haem_ATL_3
GATA3	splicing	NM_002051	c.241+1G>A	NA	10	8097860	8097860	G	A	276	0.467	Training	Haem_ATL_3
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	284	0.067	Training	Haem_ATL_3
YTHDF2	frameshift insertion	NM_016258	c.712dupT	p.A237fs	1	29069493	29069493	-	T	429	0.142	Training	Haem_ATL_4
IRF4	nonsynonymous SNV	NM_002460	c.C842T	p.T281M	6	401520	401520	C	T	228	0.031	Training	Haem_ATL_4
HLA-B	nonframeshift deletion	NM_005514	c.683_685del	p.228_229del	6	31323304	31323306	CCC	-	102	0.225	Training	Haem_ATL_4
FYN	nonsynonymous SNV	NM_002037	c.G287T	p.R96L	6	112035607	112035607	C	A	219	0.132	Training	Haem_ATL_4
CARD11	nonsynonymous SNV	NM_032415	c.T2705G	p.F902C	7	2955005	2955005	A	C	217	0.12	Training	Haem_ATL_4
GATA3	frameshift deletion	NM_002051	c.565delC	p.P189fs	10	8100591	8100591	C	-	384	0.122	Training	Haem_ATL_4
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	102	0.157	Training	Haem_ATL_4
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	131	0.382	Training	Haem_ATL_5
TBL1XR1	nonsynonymous SNV	NM_024665	c.T562C	p.S188P	3	176767925	176767925	A	G	57	0.877	Training	Haem_ATL_5
CARD11	nonsynonymous SNV	NM_032415	c.T1864C	p.S622P	7	2963943	2963943	A	G	179	0.168	Training	Haem_ATL_5
CARD11	nonsynonymous SNV	NM_032415	c.G1246A	p.E416K	7	2976766	2976766	C	T	152	0.066	Training	Haem_ATL_5
CARD11	nonsynonymous SNV	NM_032415	c.G1130A	p.R377Q	7	2977554	2977554	C	T	77	0.143	Training	Haem_ATL_5
TP53	nonsynonymous SNV	NM_000546	c.G524A	p.R175H	17	7578406	7578406	C	T	55	0.727	Training	Haem_ATL_5
CCR7	frameshift deletion	NM_001838	c.1072_1084del	p.C358fs	17	38711047	38711059	GGATGTGCCGACA	-	128	0.164	Training	Haem_ATL_5
EP300	frameshift deletion	NM_001429	c.7244_7245del	p.*2415fs	22	41574959	41574960	AG	-	60	0.15	Training	Haem_ATL_5
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	408	0.527	Training	Haem_ATL_6
HLA-B	stopgain	NM_005514	c.C535T	p.Q179X	6	31324028	31324028	G	A	69	0.203	Training	Haem_ATL_6
CARD11	nonsynonymous SNV	NM_032415	c.G2719A	p.E907K	7	2954991	2954991	C	T	221	0.032	Training	Haem_ATL_6
GATA3	stopgain	NM_002051	c.C532T	p.Q178X	10	8100558	8100558	C	T	160	0.625	Training	Haem_ATL_6
TP53	nonsynonymous SNV	NM_000546	c.T821C	p.V274A	17	7577117	7577117	A	G	79	0.468	Training	Haem_ATL_6
CCR4	stopgain	NM_005508	c.C1006T	p.Q336X	3	32995920	32995920	C	T	223	0.247	Training	Haem_ATL_7
RHOA	nonsynonymous SNV	NM_001664	c.T46C	p.C16R	3	49412977	49412977	A	G	166	0.241	Training	Haem_ATL_7
ATXN1	stopgain	NM_000332	c.C1999T	p.Q667X	6	16307009	16307009	G	A	124	0.621	Training	Haem_ATL_7
HLA-B	stopgain	NM_005514	c.G573A	p.W191X	6	31323990	31323990	C	T	64	0.312	Training	Haem_ATL_7
CARD11	nonsynonymous SNV	NM_032415	c.C1299G	p.S433R	7	2976713	2976713	G	C	126	0.143	Training	Haem_ATL_7
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	177	0.254	Training	Haem_ATL_7
TP53	nonsynonymous SNV	NM_000546	c.G746A	p.R249K	17	7577535	7577535	C	T	173	0.243	Training	Haem_ATL_7
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	193	0.383	Training	Haem_ATL_8
FYN	nonsynonymous SNV	NM_002037	c.G287A	p.R96Q	6	112035607	112035607	C	T	106	0.047	Training	Haem_ATL_8
HNRNPA2B1	splicing	NM_002137	c.964+2T>G	NA	7	26232869	26232869	A	C	59	0.746	Training	Haem_ATL_8
NOTCH1	nonsynonymous SNV	NM_017617	c.C7535T	p.P2512L	9	139390656	139390656	G	A	120	0.042	Training	Haem_ATL_8
VAV1	nonsynonymous SNV	NM_005428	c.A524T	p.E175V	19	6822306	6822306	A	T	100	0.38	Training	Haem_ATL_8
VAV1	nonsynonymous SNV	NM_005428	c.A1211G	p.K404R	19	6828857	6828857	A	G	144	0.375	Training	Haem_ATL_8
CD28	nonsynonymous SNV	NM_006139	c.C372G	p.D124E	2	204591675	204591675	C	G	1148	0.685	Training	Haem_ATL_9
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	751	0.364	Training	Haem_ATL_9
FYN	nonsynonymous SNV	NM_002037	c.A1337C	p.K446T	6	111995770	111995770	T	G	950	0.703	Training	Haem_ATL_9
RELA	nonsynonymous SNV	NM_021975	c.G115C	p.E39Q	11	65429479	65429479	C	G	407	0.314	Training	Haem_ATL_9
ZFP36L2	nonsynonymous SNV	NM_006887	c.G176A	p.S59N	2	43452767	43452767	C	T	148	0.264	Training	Haem_ATL_10
CBLB	nonsynonymous SNV	NM_001321790	c.G4A	p.A2T	3	105588229	105588229	C	T	403	0.3	Training	Haem_ATL_10
ATXN1	nonsynonymous SNV	NM_000332	c.G908A	p.R303Q	6	16327634	16327634	C	T	183	0.399	Training	Haem_ATL_10
HLA-B	stopgain	NM_005514	c.C796T	p.Q266X	6	31323193	31323193	G	A	244	0.369	Training	Haem_ATL_10
NOTCH1	frameshift deletion	NM_017617	c.7210delC	p.Q2404fs	9	139390981	139390981	G	-	410	0.261	Training	Haem_ATL_10
TP53	nonsynonymous SNV	NM_000546	c.A773G	p.E258G	17	7577508	7577508	T	C	177	0.791	Training	Haem_ATL_10
STAT3	nonsynonymous SNV	NM_003150	c.G2063A	p.R688Q	17	40474338	40474338	C	T	227	0.167	Training	Haem_ATL_10
EP300	stopgain	NM_001429	c.C2554T	p.Q852X	22	41545939	41545939	C	T	249	0.357	Training	Haem_ATL_10
IRF2BP2	nonsynonymous SNV	NM_182972	c.G581T	p.G194V	1	234744660	234744660	C	A	88	0.216	Training	Haem_ATL_11
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	389	0.807	Training	Haem_ATL_11
RHOA	nonsynonymous SNV	NM_001664	c.G481A	p.A161T	3	49397743	49397743	C	T	247	0.656	Training	Haem_ATL_11
TBL1XR1	nonsynonymous SNV	NM_024665	c.G1502A	p.S501N	3	176744177	176744177	C	T	258	0.151	Training	Haem_ATL_11
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	203	0.611	Training	Haem_ATL_11
B2M	nonsynonymous SNV	NM_004048	c.T2A	p.M1K	15	45003746	45003746	T	A	289	0.436	Training	Haem_ATL_11
PRKCB	nonsynonymous SNV	NM_002738	c.G80T	p.R27L	16	23847576	23847576	G	T	139	0.245	Training	Haem_ATL_11
PLCG1	nonframeshift deletion	NM_002660	c.2202_2222del	p.734_741del	20	39795400	39795420	TGTTGACCTCATCAGCTACTA	-	310	0.139	Training	Haem_ATL_11
RHOA	nonsynonymous SNV	NM_001664	c.G50T	p.G17V	3	49412973	49412973	C	A	202	0.05	Training	Haem_ATL_12
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	190	0.221	Training	Haem_ATL_12
TP53	nonframeshift deletion	NM_000546	c.733_735del	p.245_245del	17	7577546	7577548	GCC	-	279	0.308	Training	Haem_ATL_12
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	452	0.062	Training	Haem_ATL_13
FYN	nonsynonymous SNV	NM_002037	c.T1591C	p.Y531H	6	111982965	111982965	A	G	313	0.073	Training	Haem_ATL_13
STAT3	nonsynonymous SNV	NM_003150	c.A1919T	p.Y640F	17	40474482	40474482	T	A	434	0.055	Training	Haem_ATL_13
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	1048	0.23	Training	Haem_ATL_15
CBLB	nonsynonymous SNV	NM_170662	c.C1208T	p.S403L	3	105439090	105439090	G	A	297	0.279	Training	Haem_ATL_15
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	995	0.335	Training	Haem_ATL_15
VAV1	nonsynonymous SNV	NM_005428	c.G1666A	p.E556K	19	6833594	6833594	G	A	653	0.358	Training	Haem_ATL_15
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	885	0.288	Training	Haem_ATL_15
RHOA	nonsynonymous SNV	NM_001664	c.T46C	p.C16R	3	49412977	49412977	A	G	262	0.336	Training	Haem_ATL_16
TBL1XR1	nonsynonymous SNV	NM_024665	c.C1256T	p.S419F	3	176750919	176750919	G	A	190	0.826	Training	Haem_ATL_16
TET2	frameshift deletion	NM_017628	c.1315_1319del	p.N439fs	4	106156414	106156418	AACCA	-	270	0.322	Training	Haem_ATL_16
TET2	stopgain	NM_001127208	c.4011delT	p.Y1337X	4	106182972	106182972	T	-	203	0.498	Training	Haem_ATL_16
IRF4	nonsynonymous SNV	NM_002460	c.C208G	p.L70V	6	393360	393360	C	G	121	0.645	Training	Haem_ATL_16
FYN	nonsynonymous SNV	NM_002037	c.G1564T	p.D522Y	6	111982992	111982992	C	A	193	0.031	Training	Haem_ATL_16
FYN	nonsynonymous SNV	NM_002037	c.C526T	p.R176C	6	112025223	112025223	G	A	213	0.16	Training	Haem_ATL_16
CARD11	nonsynonymous SNV	NM_032415	c.T2705G	p.F902C	7	2955005	2955005	A	C	202	0.401	Training	Haem_ATL_16
B2M	frameshift deletion	NM_004048	c.200delA	p.E67fs	15	45007753	45007753	A	-	161	0.18	Training	Haem_ATL_16
STAT3	nonsynonymous SNV	NM_003150	c.A1973G	p.K658R	17	40474428	40474428	T	C	247	0.425	Training	Haem_ATL_16
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	262	0.37	Training	Haem_ATL_16
CSNK1A1	nonsynonymous SNV	NM_001892	c.G406A	p.D136N	5	148899903	148899903	C	T	563	0.462	Training	Haem_ATL_17
CSNK1A1	nonsynonymous SNV	NM_001892	c.C80T	p.S27F	5	148930448	148930448	G	A	1060	0.146	Training	Haem_ATL_17
STAT3	nonsynonymous SNV	NM_003150	c.G1846A	p.E616K	17	40475064	40475064	C	T	583	0.324	Training	Haem_ATL_17
VAV1	nonframeshift deletion	NM_005428	c.498_530del	p.166_177del	19	6822280	6822312	GGAGGCGGAAGGCGACGAGATCTATGAGGACCT	-	514	0.14	Training	Haem_ATL_17
PLCG1	nonframeshift deletion	NM_002660	c.2210_2221del	p.737_741del	20	39795408	39795419	TCATCAGCTACT	-	954	0.227	Training	Haem_ATL_17
PLCG1	nonsynonymous SNV	NM_002660	c.A2222C	p.Y741S	20	39795420	39795420	A	C	755	0.258	Training	Haem_ATL_17
TP53	stopgain	NM_000546	c.A193T	p.R65X	17	7579494	7579494	T	A	378	0.487	Training	Haem_ATL_18
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	702	0.303	Training	Haem_ATL_18
PLCG1	nonsynonymous SNV	NM_002660	c.A1523G	p.H508R	20	39794103	39794103	A	G	685	0.293	Training	Haem_ATL_18
PLCG1	nonframeshift deletion	NM_002660	c.2193_2195del	p.731_732del	20	39795391	39795393	CGA	-	891	0.286	Training	Haem_ATL_18
PLCG1	nonsynonymous SNV	NM_002660	c.C2196G	p.D732E	20	39795394	39795394	C	G	688	0.299	Training	Haem_ATL_18
TP53	nonsynonymous SNV	NM_000546	c.C817T	p.R273C	17	7577121	7577121	G	A	590	0.061	Training	Haem_ATL_19
VAV1	nonsynonymous SNV	NM_005428	c.G1668C	p.E556D	19	6833596	6833596	G	C	605	0.028	Training	Haem_ATL_19
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	831	0.16	Training	Haem_ATL_20
TBL1XR1	nonframeshift deletion	NM_024665	c.971_973del	p.324_325del	3	176756175	176756177	AAG	-	793	0.142	Training	Haem_ATL_20
ATXN1	stoploss	NM_000332	c.A2447G	p.X816W	6	16306561	16306561	T	C	325	0.403	Training	Haem_ATL_20
HLA-B	frameshift deletion	NM_005514	c.11_15del	p.M4fs	6	31324921	31324925	CGCCA	-	714	0.148	Training	Haem_ATL_20
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	538	0.387	Training	Haem_ATL_20
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	805	0.166	Training	Haem_ATL_20
EP300	frameshift deletion	NM_001429	c.3784_3791del	p.H1262fs	22	41560112	41560119	CATGAGAT	-	1024	0.127	Training	Haem_ATL_20
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1169G	p.H390R	3	176752067	176752067	T	C	480	0.392	Training	Haem_ATL_21
FYN	nonsynonymous SNV	NM_002037	c.C1566G	p.D522E	6	111982990	111982990	G	C	630	0.195	Training	Haem_ATL_21
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	1429	0.486	Training	Haem_ATL_21
VAV1	nonsynonymous SNV	NM_005428	c.A1493G	p.Q498R	19	6832196	6832196	A	G	441	0.422	Training	Haem_ATL_21
PLCG1	nonsynonymous SNV	NM_002660	c.A3494T	p.D1165V	20	39802391	39802391	A	T	912	0.19	Training	Haem_ATL_21
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.G964C	p.G322R	7	26232871	26232871	C	G	585	0.168	Training	Haem_ATL_22
CSNK1A1	nonsynonymous SNV	NM_001892	c.G480C	p.L160F	5	148892749	148892749	C	G	249	0.06	Training	Haem_ATL_23
IKBKB	nonsynonymous SNV	NM_001556	c.G607A	p.V203I	8	42166458	42166458	G	A	381	0.063	Training	Haem_ATL_23
PRKCB	nonsynonymous SNV	NM_002738	c.G1597A	p.E533K	16	24196495	24196495	G	A	263	0.3	Training	Haem_ATL_23
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	349	0.166	Training	Haem_ATL_23
TP53	nonsynonymous SNV	NM_000546	c.G524A	p.R175H	17	7578406	7578406	C	T	252	0.726	Training	Haem_ATL_23
CSNK2A1	nonsynonymous SNV	NM_001895	c.G935A	p.R312Q	20	468109	468109	C	T	266	0.361	Training	Haem_ATL_23
EP300	frameshift insertion	NM_001429	c.6964dupC	p.Q2321fs	22	41574678	41574678	-	C	544	0.131	Training	Haem_ATL_23
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	939	0.267	Training	Haem_ATL_24
CSNK1A1	nonsynonymous SNV	NM_001892	c.C592A	p.Q198K	5	148892637	148892637	G	T	487	0.3	Training	Haem_ATL_24
CARD11	nonsynonymous SNV	NM_032415	c.G1010A	p.R337Q	7	2978320	2978320	C	T	589	0.163	Training	Haem_ATL_24
FAS	splicing	NM_000043	c.651+2T>G	NA	10	90771840	90771840	T	G	319	0.132	Training	Haem_ATL_24
FAS	splicing	NM_000043	c.676+1G>A	NA	10	90773125	90773125	G	A	493	0.095	Training	Haem_ATL_24
PRKCB	nonsynonymous SNV	NM_002738	c.G1408C	p.D470H	16	24192124	24192124	G	C	543	0.028	Training	Haem_ATL_24
VAV1	nonsynonymous SNV	NM_005428	c.T205G	p.F69V	19	6820713	6820713	T	G	530	0.164	Training	Haem_ATL_24
POT1	stopgain	NM_015450	c.C280T	p.Q94X	7	124503670	124503670	G	A	530	0.162	Training	Haem_ATL_25

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
NOTCH1	nonsynonymous SNV	NM_017617	c.A1718C	p.D573A	9	139410120	139410120	T	G	188	0.043	Training	Haem_ATL_25
GATA3	stopgain	NM_002051	c.C189G	p.Y63X	10	8097807	8097807	C	G	900	0.159	Training	Haem_ATL_25
CCR7	stopgain	NM_001838	c.G1048T	p.E350X	17	38711083	38711083	C	A	921	0.162	Training	Haem_ATL_25
VAV1	nonsynonymous SNV	NM_005428	c.G1668C	p.E556D	19	6833596	6833596	G	C	673	0.312	Training	Haem_ATL_25
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	951	0.132	Training	Haem_ATL_25
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	2280	0.341	Training	Haem_ATL_26
CARD11	nonframeshift deletion	NM_032415	c.1846_1860del	p.616_620del	7	2963947	2963961	GGAGGAGGAGTGGAT	-	1752	0.112	Training	Haem_ATL_26
CARD11	nonsynonymous SNV	NM_032415	c.G1404C	p.R468S	7	2974201	2974201	C	G	1480	0.495	Training	Haem_ATL_26
CARD11	nonsynonymous SNV	NM_032415	c.C1071A	p.D357E	7	2977613	2977613	G	T	1622	0.202	Training	Haem_ATL_26
FAS	stopgain	NM_000043	c.T671G	p.L224X	10	90773119	90773119	T	G	917	0.256	Training	Haem_ATL_26
CCR7	frameshift deletion	NM_001838	c.1051_1054del	p.Q351fs	17	38711077	38711080	GCTG	-	2027	0.146	Training	Haem_ATL_26
EP300	stopgain	NM_001429	c.C256T	p.R86X	22	41513352	41513352	C	T	1829	0.217	Training	Haem_ATL_26
RHOA	nonsynonymous SNV	NM_001664	c.G248A	p.C83Y	3	49405890	49405890	C	T	1989	0.049	Training	Haem_ATL_27
CARD11	nonsynonymous SNV	NM_032415	c.G2203A	p.E735K	7	2962334	2962334	C	T	1503	0.058	Training	Haem_ATL_27
FAS	nonsynonymous SNV	NM_000043	c.T5A	p.L2Q	10	90750638	90750638	T	A	1566	0.059	Training	Haem_ATL_27
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1663	0.025	Training	Haem_ATL_27
PRKCB	nonsynonymous SNV	NM_002738	c.G1636A	p.E546K	16	24196802	24196802	G	A	1925	0.056	Training	Haem_ATL_27
PLCG1	nonsynonymous SNV	NM_002660	c.A3459C	p.E1153D	20	39802356	39802356	A	C	1033	0.254	Training	Haem_ATL_29
PLCG1	nonframeshift deletion	NM_002660	c.3482_3499del	p.1161_1167del	20	39802379	39802396	TGTATGAGGAAGACATGT	-	1211	0.135	Training	Haem_ATL_29
PLCG1	nonframeshift deletion	NM_002660	c.3509_3511del	p.1170_1171del	20	39802406	39802408	AGA	-	1091	0.093	Training	Haem_ATL_29
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	847	0.47	Training	Haem_ATL_30
TET2	stopgain	NM_001127208	c.G3955T	p.E1319X	4	106182916	106182916	G	T	419	0.957	Training	Haem_ATL_30
CSNK1A1	nonsynonymous SNV	NM_001892	c.G480C	p.L160F	5	148892749	148892749	C	G	450	0.916	Training	Haem_ATL_30
PRKCB	nonsynonymous SNV	NM_002738	c.G163C	p.D55H	16	23847659	23847659	G	C	727	0.285	Training	Haem_ATL_30
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	598	0.048	Training	Haem_ATL_30
VAV1	nonsynonymous SNV	NM_005428	c.G1668C	p.E556D	19	6833596	6833596	G	C	570	0.928	Training	Haem_ATL_30
IRF2BP2	nonsynonymous SNV	NM_182972	c.C943T	p.H315Y	1	234744298	234744298	G	A	51	0.294	Training	Haem_ATL_31
CCR4	nonsynonymous SNV	NM_005508	c.G98A	p.G33D	3	32995012	32995012	G	A	57	0.193	Training	Haem_ATL_31
CBLB	nonsynonymous SNV	NM_170662	c.C1208T	p.S403L	3	105439090	105439090	G	A	42	0.095	Training	Haem_ATL_31
IRF4	nonsynonymous SNV	NM_002460	c.C166T	p.H56Y	6	393318	393318	C	T	63	0.175	Training	Haem_ATL_31
IRF4	nonsynonymous SNV	NM_002460	c.C342A	p.S114R	6	394946	394946	C	A	115	0.2	Training	Haem_ATL_31
NOTCH1	stopgain	NM_017617	c.C7507T	p.Q2503X	9	139390684	139390684	G	A	66	0.242	Training	Haem_ATL_31
GATA3	stopgain	NM_002051	c.C189G	p.Y63X	10	8097807	8097807	C	G	107	0.065	Training	Haem_ATL_31
RELA	stopgain	NM_021975	c.C985T	p.R329X	11	65423207	65423207	G	A	157	0.032	Training	Haem_ATL_31
CCR7	stopgain	NM_001838	c.G1065A	p.W355X	17	38711066	38711066	C	T	98	0.153	Training	Haem_ATL_31
CSNK2A1	splicing	NM_001895	c.824+2T>C	NA	20	469320	469320	A	G	38	0.263	Training	Haem_ATL_31
CD58	splicing	NM_001779	c.628+2T>C	NA	1	117078585	117078585	A	G	196	0.878	Training	Haem_ATL_31
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	454	0.042	Training	Haem_ATL_31
HNRNPA2B1	nonframeshift insertion	NM_002137	c.905_906insCTACGG	p.G302delinsGYG	7	26232929	26232929	-	CCGTAG	1075	0.312	Training	Haem_ATL_31
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	621	0.496	Training	Haem_ATL_31
IRF2BP2	frameshift insertion	NM_182972	c.1627_1628insGGAG	p.A543fs	1	234743019	234743019	-	CTCC	395	0.289	Training	Haem_ATL_32
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	179	0.352	Training	Haem_ATL_32
IKBKB	nonsynonymous SNV	NM_001556	c.G607A	p.V203I	8	42166458	42166458	G	A	238	0.311	Training	Haem_ATL_32
NOTCH1	nonsynonymous SNV	NM_017617	c.G5161A	p.V1721M	9	139397640	139397640	C	T	258	0.357	Training	Haem_ATL_32
GPR183	frameshift deletion	NM_004951	c.748_751del	p.I250fs	13	99947649	99947652	CAAT	-	349	0.223	Training	Haem_ATL_32
NFKBIA	frameshift deletion	NM_020529	c.131_159del	p.Q44fs	14	35873692	35873720	GCGGATCTCCTGCAGCTCCTTGACCATCT	-	519	0.183	Training	Haem_ATL_32
CCR7	stopgain	NM_001838	c.C1051T	p.Q351X	17	38711080	38711080	G	A	269	0.323	Training	Haem_ATL_32
VAV1	nonsynonymous SNV	NM_005428	c.G2393C	p.R798P	19	6854018	6854018	G	C	223	0.278	Training	Haem_ATL_32
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	293	0.311	Training	Haem_ATL_32
NOTCH1	frameshift deletion	NM_017617	c.6427_6436del	p.N2143fs	9	139391755	139391764	GGTAGCCGTT	-	871	0.392	Training	Haem_ATL_32
GATA3	splicing	NM_002051	c.241+1G>C	NA	10	8097860	8097860	G	C	686	0.42	Training	Haem_ATL_32
PRKCB	nonsynonymous SNV	NM_002738	c.A1637T	p.E546V	16	24196803	24196803	A	T	570	0.133	Training	Haem_ATL_32
ZNF638	nonsynonymous SNV	NM_014497	c.A508G	p.M170V	2	71576592	71576592	A	G	411	0.292	Training	Haem_ATL_33
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1388T	p.D463V	3	176750787	176750787	T	A	365	0.236	Training	Haem_ATL_33
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	197	0.284	Training	Haem_ATL_33
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.G964A	p.G322R	7	26232871	26232871	C	T	312	0.24	Training	Haem_ATL_33
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	276	0.116	Training	Haem_ATL_33
CCR7	stopgain	NM_001838	c.C1051T	p.Q351X	17	38711080	38711080	G	A	387	0.274	Training	Haem_ATL_33
STAT3	nonsynonymous SNV	NM_003150	c.A1973G	p.K658R	17	40474428	40474428	T	C	380	0.218	Training	Haem_ATL_33
VAV1	nonsynonymous SNV	NM_005428	c.G2393C	p.R798P	19	6854018	6854018	G	C	321	0.262	Training	Haem_ATL_33
CCR4	frameshift insertion	NM_005508	c.967dupA	p.C322fs	3	32995880	32995880	-	A	598	0.273	Training	Haem_ATL_34
CSNK1A1	nonsynonymous SNV	NM_001892	c.A1000G	p.M334V	5	148885016	148885016	T	C	377	0.318	Training	Haem_ATL_34
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	259	0.054	Training	Haem_ATL_34
TNFAIP3	frameshift insertion	NM_006290	c.318dupT	p.H106fs	6	138196003	138196003	-	T	387	0.178	Training	Haem_ATL_34
CARD11	nonsynonymous SNV	NM_032415	c.T346C	p.S116P	7	2985465	2985465	A	G	308	0.305	Training	Haem_ATL_34
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	478	0.469	Training	Haem_ATL_34
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	456	0.272	Training	Haem_ATL_34
PLCG1	nonsynonymous SNV	NM_002660	c.G2258A	p.R753H	20	39795456	39795456	G	A	413	0.177	Training	Haem_ATL_34
CD58	nonsynonymous SNV	NM_001779	c.T419A	p.V140D	1	117078796	117078796	A	T	732	0.253	Training	Haem_ATL_35
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	587	0.31	Training	Haem_ATL_35
NOTCH1	stopgain	NM_017617	c.C7330T	p.Q2444X	9	139390861	139390861	G	A	483	0.151	Training	Haem_ATL_35
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	834	0.044	Training	Haem_ATL_35
PRKCB	nonsynonymous SNV	NM_002738	c.A1889G	p.D630G	16	24226004	24226004	A	G	1208	0.105	Training	Haem_ATL_35
CCR7	stopgain	NM_001838	c.C1045T	p.Q349X	17	38711086	38711086	G	A	1017	0.193	Training	Haem_ATL_35
TBL1XR1	nonsynonymous SNV	NM_024665	c.C919G	p.H307D	3	176763923	176763923	G	C	553	0.217	Training	Haem_ATL_36
IRF4	nonsynonymous SNV	NM_002460	c.G358A	p.D120N	6	394962	394962	G	A	790	0.265	Training	Haem_ATL_36
TP53	nonsynonymous SNV	NM_000546	c.C817T	p.R273C	17	7577121	7577121	G	A	726	0.146	Training	Haem_ATL_36
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	584	0.125	Training	Haem_ATL_36
CCR4	stopgain	NM_005508	c.C1034A	p.S345X	3	32995948	32995948	C	A	938	0.281	Training	Haem_ATL_37
CBLB	nonsynonymous SNV	NM_170662	c.G38A	p.R13Q	3	105586384	105586384	C	T	768	0.24	Training	Haem_ATL_37
HNRNPA2B1	splicing	NM_002137	c.964+1G>A	NA	7	26232870	26232870	C	T	819	0.253	Training	Haem_ATL_37
TP53	stopgain	NM_000546	c.G437A	p.W146X	17	7578493	7578493	C	T	536	0.36	Training	Haem_ATL_37
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	972	0.244	Training	Haem_ATL_37
CSNK1A1	nonframeshift deletion	NM_001892	c.334_339del	p.112_113del	5	148904626	148904631	TACAGT	-	1398	0.28	Training	Haem_ATL_38
CSNK1A1	nonsynonymous SNV	NM_001892	c.C80G	p.S27C	5	148930448	148930448	G	C	1080	0.3	Training	Haem_ATL_38
TP53	nonsynonymous SNV	NM_000546	c.G733A	p.G245S	17	7577548	7577548	C	T	823	0.122	Training	Haem_ATL_38
CCR7	stopgain	NM_001838	c.C1045T	p.Q349X	17	38711086	38711086	G	A	1098	0.067	Training	Haem_ATL_38
STAT3	nonframeshift deletion	NM_003150	c.1847_1849del	p.616_617del	17	40475061	40475063	CTT	-	1189	0.292	Training	Haem_ATL_38
STAT3	nonsynonymous SNV	NM_003150	c.A1847G	p.E616G	17	40475063	40475063	T	C	618	0.045	Training	Haem_ATL_38
VAV1	frameshift deletion	NM_005428	c.2305_2320del	p.E769fs	19	6853063	6853078	GAAAAGAGAACCATCA	-	1226	0.139	Training	Haem_ATL_38
VAV1	stopgain	NM_005428	c.2324_2325insGTAGGA	p.R775delinsRX	19	6853082	6853082	-	GTAGGA	992	0.17	Training	Haem_ATL_38
PLCG1	nonsynonymous SNV	NM_002660	c.A1817G	p.Q606R	20	39794851	39794851	A	G	745	0.042	Training	Haem_ATL_38
IRF2BP2	nonsynonymous SNV	NM_182972	c.C488T	p.S163F	1	234744753	234744753	G	A	238	0.395	Training	Haem_ATL_39
IRF2BP2	nonsynonymous SNV	NM_182972	c.G288T	p.Q96H	1	234744953	234744953	C	A	167	0.329	Training	Haem_ATL_39
IRF2BP2	frameshift deletion	NM_182972	c.107_119del	p.V36fs	1	234745122	234745134	CAGCCGCGGCAGA	-	1058	0.296	Training	Haem_ATL_39
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	1939	0.259	Training	Haem_ATL_39
RHOA	nonsynonymous SNV	NM_001664	c.T46C	p.C16R	3	49412977	49412977	A	G	1860	0.244	Training	Haem_ATL_39
IRF4	nonsynonymous SNV	NM_002460	c.G341A	p.S114N	6	394945	394945	G	A	1575	0.546	Training	Haem_ATL_39
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.A937G	p.R313G	7	26232898	26232898	T	C	1197	0.369	Training	Haem_ATL_39
CDKN2A	stopgain	NM_000077	c.C387A	p.Y129X	9	21970971	21970971	G	T	398	0.583	Training	Haem_ATL_39
NFKBIA	stopgain	NM_020529	c.C148T	p.Q50X	14	35873703	35873703	G	A	1190	0.376	Training	Haem_ATL_39
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	1901	0.55	Training	Haem_ATL_39
VAV1	nonsynonymous SNV	NM_005428	c.C2368T	p.R790C	19	6853993	6853993	C	T	1220	0.376	Training	Haem_ATL_39
CSNK2A1	splicing	NM_001895	c.622-2A>G	NA	20	470527	470527	T	C	999	0.733	Training	Haem_ATL_39
IRF2BP2	nonsynonymous SNV	NM_182972	c.G116A	p.G39D	1	234745125	234745125	C	T	740	0.391	Training	Haem_ATL_40
CD28	nonsynonymous SNV	NM_006139	c.T151A	p.F51I	2	204591454	204591454	T	A	2053	0.058	Training	Haem_ATL_40
CCR4	frameshift insertion	NM_005508	c.974dupT	p.L325fs	3	32995887	32995887	-	T	2464	0.377	Training	Haem_ATL_40
CARD11	nonsynonymous SNV	NM_032415	c.G367A	p.G123S	7	2984163	2984163	C	T	700	0.326	Training	Haem_ATL_40
IKBKB	nonsynonymous SNV	NM_001556	c.G607A	p.V203I	8	42166458	42166458	G	A	1095	0.395	Training	Haem_ATL_40
GATA3	frameshift deletion	NM_002051	c.702_703del	p.F234fs	10	8100728	8100729	CC	-	2163	0.371	Training	Haem_ATL_40
FAS	frameshift insertion	NM_000043	c.691dupA	p.S230fs	10	90773889	90773889	-	A	1659	0.414	Training	Haem_ATL_40
CCR4	nonsynonymous SNV	NM_005508	c.G1018C	p.A340P	3	32995932	32995932	G	C	1037	0.147	Training	Haem_ATL_41
TBL1XR1	nonsynonymous SNV	NM_024665	c.G740A	p.G247E	3	176765300	176765300	C	T	704	0.183	Training	Haem_ATL_41
IRF4	nonsynonymous SNV	NM_002460	c.G341A	p.S114N	6	394945	394945	G	A	1677	0.487	Training	Haem_ATL_41
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	1154	0.181	Training	Haem_ATL_41
TP53	nonsynonymous SNV	NM_000546	c.C523G	p.R175G	17	7578407	7578407	G	C	933	0.354	Training	Haem_ATL_41
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	680	0.21	Training	Haem_ATL_41
CBLB	nonframeshift deletion	NM_170662	c.1126_1155del	p.376_385del	3	105452901	105452930	AATCTTGACATCTTTGTCATTCTCTGCACA	-	2043	0.16	Training	Haem_ATL_42
TBL1XR1	nonsynonymous SNV	NM_024665	c.G1387C	p.D463H	3	176750788	176750788	C	G	1249	0.247	Training	Haem_ATL_42
TBL1XR1	nonsynonymous SNV	NM_024665	c.G1177A	p.E393K	3	176752059	176752059	C	T	1066	0.264	Training	Haem_ATL_42
CSNK2B	stopgain	NM_001320	c.563dupA	p.Y188_G189delinsX	6	31637617	31637617	-	A	1388	0.24	Training	Haem_ATL_42
POT1	frameshift deletion	NM_015450	c.20delC	p.T7fs	7	124532424	124532424	G	-	1774	0.227	Training	Haem_ATL_42
GATA3	frameshift insertion	NM_002051	c.561dupG	p.Q187fs	10	8100586	8100586	-	G	1311	0.108	Training	Haem_ATL_42
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	1590	0.477	Training	Haem_ATL_42
CCR4	frameshift insertion	NM_005508	c.974dupT	p.L325fs	3	32995887	32995887	-	T	2228	0.399	Training	Haem_ATL_43
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	1111	0.451	Training	Haem_ATL_43
POT1	nonsynonymous SNV	NM_015450	c.G818A	p.R273Q	7	124493077	124493077	C	T	1081	0.448	Training	Haem_ATL_43
NOTCH1	frameshift deletion	NM_017617	c.7541_7542del	p.P2514fs	9	139390649	139390650	AG	-	1376	0.421	Training	Haem_ATL_43
TP53	nonsynonymous SNV	NM_000546	c.G711A	p.M237I	17	7577570	7577570	C	T	494	0.891	Training	Haem_ATL_43
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	733	0.034	Training	Haem_ATL_44
TP53	frameshift deletion	NM_000546	c.1146delA	p.K382fs	17	7572963	7572963	T	-	817	0.376	Training	Haem_ATL_44
TP53	nonsynonymous SNV	NM_000546	c.A718C	p.S240R	17	7577563	7577563	T	G	607	0.359	Training	Haem_ATL_44

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
PLCG1	nonframeshift deletion	NM_002660	c.3484_3501del	p.1162_1167del	20	39802381	39802398	TATGAGGAAGACATGTTT	-	1129	0.18	Training	Haem_ATL_44
PLCG1	nonframeshift deletion	NM_002660	c.3509_3511del	p.1170_1171del	20	39802406	39802408	AGA	-	1139	0.065	Training	Haem_ATL_44
CD58	nonsynonymous SNV	NM_001779	c.C507G	p.N169K	1	117078708	117078708	G	C	939	0.103	Training	Haem_ATL_45
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1190	0.171	Training	Haem_ATL_45
IRF2BP2	nonsynonymous SNV	NM_182972	c.G581A	p.G194D	1	234744660	234744660	C	T	118	0.458	Training	Haem_ATL_46
TP53	stopgain	NM_000546	c.C637T	p.R213X	17	7578212	7578212	G	A	559	0.767	Training	Haem_ATL_46
VAV1	nonsynonymous SNV	NM_005428	c.A1501T	p.M501L	19	6832204	6832204	A	T	662	0.477	Training	Haem_ATL_46
ATXN1	nonsynonymous SNV	NM_000332	c.C13G	p.Q5E	6	16328529	16328529	G	C	553	0.269	Training	Haem_ATL_47
CARD11	nonsynonymous SNV	NM_032415	c.T1079A	p.M360K	7	2977605	2977605	A	T	1314	0.072	Training	Haem_ATL_47
CARD11	nonsynonymous SNV	NM_032415	c.A1078G	p.M360V	7	2977606	2977606	T	C	1321	0.32	Training	Haem_ATL_47
GATA3	stopgain	NM_002051	c.C559T	p.Q187X	10	8100585	8100585	C	T	1254	0.383	Training	Haem_ATL_47
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	707	0.388	Training	Haem_ATL_47
PLCG1	nonsynonymous SNV	NM_002660	c.A1526G	p.Y509C	20	39794106	39794106	A	G	1226	0.301	Training	Haem_ATL_47
PLCG1	nonsynonymous SNV	NM_002660	c.G2606A	p.G869E	20	39798122	39798122	G	A	1148	0.075	Training	Haem_ATL_47
NOTCH1	stopgain	NM_017617	c.C7027T	p.Q2343X	9	139391164	139391164	G	A	245	0.278	Training	Haem_ATL_48
TP53	nonsynonymous SNV	NM_000546	c.G814A	p.V272M	17	7577124	7577124	C	T	341	0.933	Training	Haem_ATL_48
JAK3	nonsynonymous SNV	NM_000215	c.G1533A	p.M511I	19	17949108	17949108	C	T	282	0.404	Training	Haem_ATL_48
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	567	0.33	Training	Haem_ATL_49
PLCG1	nonsynonymous SNV	NM_002660	c.T2603C	p.L868P	20	39798119	39798119	T	C	1093	0.328	Training	Haem_ATL_49
PIK3CD	splicing	NM_005026	c.1812-2A>G	NA	1	9781500	9781500	A	G	384	0.341	Training	Haem_ATL_50
IRF2BP2	nonsynonymous SNV	NM_182972	c.C641T	p.A214V	1	234744600	234744600	G	A	148	0.061	Training	Haem_ATL_50
IRF2BP2	nonsynonymous SNV	NM_182972	c.G294C	p.Q98H	1	234744947	234744947	C	G	171	0.181	Training	Haem_ATL_50
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	1528	0.258	Training	Haem_ATL_50
FYN	nonsynonymous SNV	NM_002037	c.A71G	p.Q24R	6	112041184	112041184	T	C	1009	0.232	Training	Haem_ATL_50
FAS	nonsynonymous SNV	NM_000043	c.T725C	p.L242P	10	90773924	90773924	T	C	1572	0.278	Training	Haem_ATL_50
VAV1	nonsynonymous SNV	NM_005428	c.G1668T	p.E556D	19	6833596	6833596	G	T	1021	0.524	Training	Haem_ATL_50
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	552	0.277	Training	Haem_ATL_50
RHOA	nonsynonymous SNV	NM_001664	c.G248A	p.C83Y	3	49405890	49405890	C	T	1452	0.211	Training	Haem_ATL_51
IRF4	nonsynonymous SNV	NM_002460	c.G104A	p.G35D	6	393256	393256	G	A	990	0.311	Training	Haem_ATL_51
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	1109	0.335	Training	Haem_ATL_51
FAS	nonsynonymous SNV	NM_000043	c.A816T	p.E272D	10	90774015	90774015	A	T	1114	0.373	Training	Haem_ATL_51
GPR183	frameshift deletion	NM_004951	c.172_173del	p.Q58fs	13	99948227	99948228	TG	-	964	0.507	Training	Haem_ATL_51
ZFP36L2	nonsynonymous SNV	NM_006887	c.C772G	p.L258V	2	43452171	43452171	G	C	114	0.325	Training	Haem_ATL_52
CCR4	frameshift insertion	NM_005508	c.997dupG	p.C332fs	3	32995910	32995910	-	G	295	0.607	Training	Haem_ATL_52
RHOA	nonsynonymous SNV	NM_001664	c.T46C	p.C16R	3	49412977	49412977	A	G	203	0.138	Training	Haem_ATL_52
TBL1XR1	nonsynonymous SNV	NM_024665	c.G974T	p.C325F	3	176756174	176756174	C	A	151	0.225	Training	Haem_ATL_52
PDE7B	nonsynonymous SNV	NM_018945	c.G257C	p.R86P	6	136468579	136468579	G	C	118	0.305	Training	Haem_ATL_52
NOTCH1	stopgain	NM_017617	c.C7183T	p.Q2395X	9	139391008	139391008	G	A	162	0.241	Training	Haem_ATL_52
B2M	frameshift deletion	NM_004048	c.136_137del	p.Y46fs	15	45007689	45007690	TA	-	183	0.306	Training	Haem_ATL_52
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	146	0.301	Training	Haem_ATL_52
CCR7	stopgain	NM_001838	c.G1065A	p.W355X	17	38711066	38711066	C	T	169	0.32	Training	Haem_ATL_52
STAT3	nonsynonymous SNV	NM_003150	c.A1982T	p.D661V	17	40474419	40474419	T	A	152	0.118	Training	Haem_ATL_52
STAT3	nonframeshift deletion	NM_003150	c.1847_1849del	p.616_617del	17	40475061	40475063	CTT	-	238	0.223	Training	Haem_ATL_52
STAT3	nonsynonymous SNV	NM_003150	c.A1847G	p.E616G	17	40475063	40475063	T	C	133	0.045	Training	Haem_ATL_52
VAV1	nonsynonymous SNV	NM_005428	c.G2389A	p.D797N	19	6854014	6854014	G	A	154	0.156	Training	Haem_ATL_52
VAV1	nonsynonymous SNV	NM_005428	c.A2443G	p.K815E	19	6854068	6854068	A	G	141	0.319	Training	Haem_ATL_52
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	146	0.11	Training	Haem_ATL_52
FAS	nonsynonymous SNV	NM_000043	c.G778A	p.D260N	10	90773977	90773977	G	A	1717	0.088	Training	Haem_ATL_53
TBL1XR1	nonsynonymous SNV	NM_024665	c.A920G	p.H307R	3	176763922	176763922	T	C	947	0.032	Training	Haem_ATL_54
TBL1XR1	nonsynonymous SNV	NM_024665	c.T716C	p.L239P	3	176765324	176765324	A	G	1561	0.224	Training	Haem_ATL_55
IRF4	nonsynonymous SNV	NM_002460	c.G309C	p.K103N	6	394913	394913	G	C	2189	0.244	Training	Haem_ATL_55
IRF4	nonsynonymous SNV	NM_002460	c.G341A	p.S114N	6	394945	394945	G	A	1921	0.28	Training	Haem_ATL_55
IRF4	nonsynonymous SNV	NM_002460	c.C342G	p.S114R	6	394946	394946	C	G	1938	0.276	Training	Haem_ATL_55
GATA3	nonframeshift insertion	NM_002051	c.499_500insTGT	p.L167delinsLL	10	8100525	8100525	-	TGT	2894	0.352	Training	Haem_ATL_55
STAT3	nonframeshift deletion	NM_003150	c.1847_1849del	p.616_617del	17	40475061	40475063	CTT	-	1946	0.18	Training	Haem_ATL_55
VAV1	nonsynonymous SNV	NM_005428	c.G2389A	p.D797N	19	6854014	6854014	G	A	1839	0.214	Training	Haem_ATL_55
GPR183	stopgain	NM_004951	c.C259T	p.R87X	13	99948141	99948141	G	A	1964	0.512	Training	Haem_ATL_56
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1458	0.188	Training	Haem_ATL_56
STAT3	nonsynonymous SNV	NM_003150	c.G1852C	p.G618R	17	40475058	40475058	C	G	1479	0.222	Training	Haem_ATL_56
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	909	0.239	Training	Haem_ATL_56
PLCG1	nonsynonymous SNV	NM_002660	c.A3506G	p.D1169G	20	39802403	39802403	A	G	2003	0.215	Training	Haem_ATL_56
IRF2BP2	nonsynonymous SNV	NM_182972	c.G524A	p.S175N	1	234744717	234744717	C	T	359	0.036	Training	Haem_ATL_57
TP53	nonsynonymous SNV	NM_000546	c.G814A	p.V272M	17	7577124	7577124	C	T	1610	0.089	Training	Haem_ATL_57
PIK3CD	frameshift deletion	NM_005026	c.952_967del	p.S318fs	1	9777616	9777631	TCCCTGGAGCAGCCGT	-	1524	0.262	Training	Haem_ATL_58
CCR4	nonframeshift deletion	NM_005508	c.1003_1017del	p.335_339del	3	32995917	32995931	CTCCAAATTTACTCT	-	2534	0.258	Training	Haem_ATL_58
HLA-B	frameshift insertion	NM_005514	c.891dupA	p.W298fs	6	31323097	31323097	-	T	2439	0.246	Training	Haem_ATL_58
POT1	nonsynonymous SNV	NM_015450	c.G703T	p.V235F	7	124493192	124493192	C	A	1272	0.332	Training	Haem_ATL_58
TP53	nonsynonymous SNV	NM_000546	c.A503G	p.H168R	17	7578427	7578427	T	C	1024	0.506	Training	Haem_ATL_58
CCR4	frameshift insertion	NM_005508	c.967dupA	p.C322fs	3	32995880	32995880	-	A	1753	0.335	Training	Haem_ATL_59
IRF4	nonsynonymous SNV	NM_002460	c.G358C	p.D120H	6	394962	394962	G	C	1031	0.328	Training	Haem_ATL_59
CARD11	nonsynonymous SNV	NM_032415	c.C1267T	p.R423W	7	2976745	2976745	G	A	1355	0.523	Training	Haem_ATL_59
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1029	0.351	Training	Haem_ATL_59
TBL1XR1	frameshift deletion	NM_024665	c.319delC	p.Q107fs	3	176769400	176769400	G	-	1610	0.912	Training	Haem_ATL_60
TBL1XR1	nonsynonymous SNV	NM_024665	c.C319A	p.Q107K	3	176769400	176769400	G	T	112	0.348	Training	Haem_ATL_60
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	1131	0.442	Training	Haem_ATL_60
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1121	0.483	Training	Haem_ATL_60
VAV1	frameshift deletion	NM_005428	c.2333_2342del	p.V778fs	19	6853946	6853967	CTCTCTCCACAGTGGGAAGCAC	-	894	0.724	Training	Haem_ATL_60
VAV1	nonsynonymous SNV	NM_005428	c.G2346T	p.K782N	19	6853971	6853971	G	T	667	0.891	Training	Haem_ATL_60
CARD11	nonsynonymous SNV	NM_032415	c.C1071G	p.D357E	7	2977613	2977613	G	C	1452	0.433	Training	Haem_ATL_61
HNRNPA2B1	splicing	NM_002137	c.842-2A>T	NA	7	26232995	26232995	T	A	1599	0.458	Training	Haem_ATL_61
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.T74G	p.L25W	7	26237285	26237285	A	C	1712	0.376	Training	Haem_ATL_61
CDKN2A	splicing	NM_000077	c.151-1G>A	NA	9	21971208	21971208	C	T	172	0.273	Training	Haem_ATL_61
EP300	nonsynonymous SNV	NM_001429	c.C123G	p.H41Q	22	41513219	41513219	C	G	1382	0.138	Training	Haem_ATL_61
CCR4	frameshift deletion	NM_005508	c.1000_1019del	p.L334fs	3	32995914	32995933	CTCCTCCAAATTTACTCTGC	-	2300	0.266	Training	Haem_ATL_62
CCR4	nonframeshift deletion	NM_005508	c.1022_1027del	p.341_343del	3	32995936	32995941	ACACCC	-	1539	0.399	Training	Haem_ATL_62
RHOA	nonsynonymous SNV	NM_001664	c.G47A	p.C16Y	3	49412976	49412976	C	T	2113	0.032	Training	Haem_ATL_62
TBL1XR1	splicing	NM_024665	c.1122+1G>A	NA	3	176755885	176755885	C	T	1713	0.693	Training	Haem_ATL_62
HLA-B	splicing	NM_005514	c.1012+1G>A	NA	6	31322883	31322883	C	T	986	0.381	Training	Haem_ATL_62
HLA-B	nonsynonymous SNV	NM_005514	c.G1012A	p.G338S	6	31322884	31322884	C	T	990	0.38	Training	Haem_ATL_62
GATA3	frameshift insertion	NM_002051	c.149dupT	p.L50fs	10	8097766	8097766	-	T	1609	0.228	Training	Haem_ATL_62
TP53	nonsynonymous SNV	NM_000546	c.G711A	p.M237I	17	7577570	7577570	C	T	1289	0.282	Training	Haem_ATL_62
TP53	splicing	NM_000546	c.673-2A>C	NA	17	7577610	7577610	T	G	1125	0.289	Training	Haem_ATL_62
CCR7	stopgain	NM_001838	c.G1065A	p.W355X	17	38711066	38711066	C	T	1581	0.148	Training	Haem_ATL_62
SETD2	nonsynonymous SNV	NM_014159	c.G361A	p.G121S	3	47165765	47165765	C	T	1061	0.287	Training	Haem_ATL_63
RHOA	nonsynonymous SNV	NM_001664	c.G50T	p.G17V	3	49412973	49412973	C	A	973	0.295	Training	Haem_ATL_63
CSNK2B	stopgain	NM_001320	c.G517T	p.E173X	6	31637245	31637245	G	T	558	0.434	Training	Haem_ATL_63
FYN	nonsynonymous SNV	NM_002037	c.C526T	p.R176C	6	112025223	112025223	G	A	587	0.484	Training	Haem_ATL_63
POT1	frameshift deletion	NM_015450	c.125_125del	p.D42fs	7	124511095	124511099	TCTGG	-	874	0.437	Training	Haem_ATL_63
ZEB1	frameshift insertion	NM_030751	c.1570dupG	p.E523fs	10	31809832	31809832	-	G	728	0.537	Training	Haem_ATL_63
EP300	nonsynonymous SNV	NM_001429	c.C5006T	p.T1669I	22	41572477	41572477	C	T	587	0.394	Training	Haem_ATL_63
CD58	stopgain	NM_001779	c.C596A	p.S199X	1	117078619	117078619	G	T	632	0.546	Training	Haem_ATL_64
IRF2BP2	nonsynonymous SNV	NM_182972	c.C925G	p.L309V	1	234744316	234744316	G	C	577	0.321	Training	Haem_ATL_64
IRF2BP2	nonsynonymous SNV	NM_182972	c.C247G	p.P83A	1	234744994	234744994	G	C	402	0.368	Training	Haem_ATL_64
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1176	0.332	Training	Haem_ATL_64
HLA-B	frameshift insertion	NM_005514	c.611_612insAC	p.E204fs	6	31323951	31323951	-	GT	323	0.529	Training	Haem_ATL_64
HNRNPA2B1	frameshift deletion	NM_002137	c.116_117del	p.V39fs	7	26237242	26237243	CA	-	1460	0.303	Training	Haem_ATL_64
GATA3	splicing	NM_002051	c.242-2A>C	NA	10	8100266	8100266	A	C	520	0.5	Training	Haem_ATL_64
NFKBIA	stopgain	NM_020529	c.C130T	p.Q44X	14	35873721	35873721	G	A	1113	0.331	Training	Haem_ATL_64
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	968	0.357	Training	Haem_ATL_64
CD58	stopgain	NM_001779	c.C593A	p.S198X	1	117078622	117078622	G	T	852	0.15	Training	Haem_ATL_65
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	2023	0.189	Training	Haem_ATL_65
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1109G	p.D370G	3	176755899	176755899	T	C	1281	0.208	Training	Haem_ATL_65
TBL1XR1	stopgain	NM_024665	c.423_424insTA	p.A142_N143delinsX	3	176769295	176769295	-	TA	1339	0.096	Training	Haem_ATL_65
VAV1	nonsynonymous SNV	NM_005428	c.G2393A	p.R798Q	19	6854018	6854018	G	A	1256	0.126	Training	Haem_ATL_65
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	867	0.122	Training	Haem_ATL_65
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	1443	0.139	Training	Haem_ATL_65
IRF2BP2	nonsynonymous SNV	NM_182972	c.G1291A	p.V431I	1	234743356	234743356	C	T	1503	0.194	Training	Haem_ATL_67
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1413	0.193	Training	Haem_ATL_67
FAS	splicing	NM_000043	c.196+2T>G	NA	10	90762953	90762953	T	G	974	0.167	Training	Haem_ATL_67
FAS	nonsynonymous SNV	NM_000043	c.A779G	p.D260G	10	90773978	90773978	A	G	938	0.198	Training	Haem_ATL_67
PLCG1	nonsynonymous SNV	NM_002660	c.C2257T	p.R753C	20	39795455	39795455	C	T	1447	0.176	Training	Haem_ATL_67
PLCG1	nonframeshift deletion	NM_002660	c.3504_3506del	p.1168_1169del	20	39802401	39802403	TGA	-	2085	0.165	Training	Haem_ATL_67
RHOA	nonsynonymous SNV	NM_001664	c.G47T	p.C16F	3	49412976	49412976	C	A	2301	0.062	Training	Haem_ATL_68
TBL1XR1	nonsynonymous SNV	NM_024665	c.A503G	p.H168R	3	176768323	176768323	T	C	2007	0.075	Training	Haem_ATL_68
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	1458	0.047	Training	Haem_ATL_68
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	2853	0.025	Training	Haem_ATL_68
IRF2BP2	nonsynonymous SNV	NM_182972	c.C641T	p.A214V	1	234744600	234744600	G	A	650	0.349	Training	Haem_ATL_69
NOTCH1	stopgain	NM_017617	c.C7246T	p.Q2416X	9	139390945	139390945	G	A	1866	0.448	Training	Haem_ATL_69
TP53	nonsynonymous SNV	NM_000546	c.C742T	p.R248W	17	7577539	7577539	G	A	882	0.783	Training	Haem_ATL_69
CCR7	stopgain	NM_001838	c.G1048T	p.E350X	17	38711083	38711083	C	A	1884	0.443	Training	Haem_ATL_69
IRF2BP2	nonsynonymous SNV	NM_182972	c.G1060T	p.A354S	1	234743587	234743587	C	A	215	0.247	Training	Haem_ATL_70
IRF2BP2	nonsynonymous SNV	NM_182972	c.G581T	p.G194V	1	234744660	234744660	C	A	204	0.299	Training	Haem_ATL_70

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	829	0.118	Training	Haem_ATL_70
RHOA	nonsynonymous SNV	NM_001664	c.G481C	p.A161P	3	49397743	49397743	C	G	464	0.034	Training	Haem_ATL_70
CSNK1A1	nonsynonymous SNV	NM_001892	c.A407G	p.D136G	5	148899902	148899902	T	C	683	0.441	Training	Haem_ATL_70
CSNK1A1	nonsynonymous SNV	NM_001892	c.C80T	p.S27F	5	148930448	148930448	G	A	442	0.287	Training	Haem_ATL_70
PRKCB	nonsynonymous SNV	NM_002738	c.A1054G	p.S352G	16	24135291	24135291	A	G	439	0.219	Training	Haem_ATL_70
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	311	0.058	Training	Haem_ATL_70
VAV1	nonsynonymous SNV	NM_005428	c.G2044A	p.E682K	19	6848040	6848040	G	A	331	0.063	Training	Haem_ATL_70
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	384	0.464	Training	Haem_ATL_70
PLCG1	nonframeshift deletion	NM_002660	c.2178_2195del	p.726_732del	20	39795376	39795393	AGGGAACTCGGAGTTCGA	-	493	0.312	Training	Haem_ATL_70
IRF4	nonsynonymous SNV	NM_002460	c.C208G	p.L70V	6	393360	393360	C	G	2610	0.027	Training	Haem_ATL_71
NOTCH1	stopgain	NM_017617	c.G7306T	p.G2436X	9	139390885	139390885	C	A	2273	0.324	Training	Haem_ATL_71
CCR7	stopgain	NM_001838	c.C1060T	p.Q354X	17	38711071	38711071	G	A	3176	0.346	Training	Haem_ATL_71
POT1	nonsynonymous SNV	NM_015450	c.C817T	p.R273W	7	124493078	124493078	G	A	1632	0.559	Training	Haem_ATL_72
NOTCH1	frameshift insertion	NM_017617	c.7535dupC	p.P2512fs	9	139390655	139390655	-	G	4744	0.169	Training	Haem_ATL_72
GATA3	frameshift insertion	NM_002051	c.249_250insGT	p.Q83fs	10	8100275	8100275	-	GT	1870	0.336	Training	Haem_ATL_72
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1993	0.029	Training	Haem_ATL_72
TP53	frameshift deletion	NM_000546	c.105_133del	p.L35fs	17	7579554	7579582	GCATCAAATCATCCATTGCTTGGGACGGC	-	1246	0.201	Training	Haem_ATL_72
CCR7	stopgain	NM_001838	c.G1065A	p.W355X	17	38711066	38711066	C	T	2281	0.299	Training	Haem_ATL_72
PLCG1	nonsynonymous SNV	NM_002660	c.G139A	p.E47K	20	39766420	39766420	G	A	1378	0.065	Training	Haem_ATL_72
PLCG1	nonsynonymous SNV	NM_002660	c.C1559T	p.S520F	20	39794139	39794139	C	T	2175	0.091	Training	Haem_ATL_72
CD58	frameshift deletion	NM_001779	c.352_355del	p.L118fs	1	117086942	117086945	AAAG	-	883	0.085	Training	Haem_ATL_73
CCR4	frameshift insertion	NM_005508	c.987dupC	p.C329fs	3	32995900	32995900	-	C	2656	0.187	Training	Haem_ATL_73
TBL1XR1	splicing	NM_024665	c.1122+2T>C	NA	3	176755884	176755884	A	G	1407	0.178	Training	Haem_ATL_73
CARD11	nonsynonymous SNV	NM_032415	c.A1078G	p.M360V	7	2977606	2977606	T	C	1738	0.09	Training	Haem_ATL_73
NOTCH1	nonsynonymous SNV	NM_017617	c.G5471A	p.R1824Q	9	139396454	139396454	C	T	1908	0.374	Training	Haem_ATL_73
FAS	frameshift deletion	NM_000043	c.690_724del	p.S230fs	10	90773889	90773923	TAAATATATCACCACTATTGCTGGAGTCATGACAC	-	721	0.026	Training	Haem_ATL_73
PLCG1	nonframeshift deletion	NM_002660	c.3502_3507del	p.1168_1169del	20	39802399	39802404	AGTGAC	-	2765	0.149	Training	Haem_ATL_73
YTHDF2	stopgain	NM_016258	c.C424T	p.Q142X	1	29069206	29069206	C	T	1076	0.464	Training	Haem_ATL_74
CCR4	frameshift deletion	NM_005508	c.980_993del	p.V327fs	3	32995894	32995907	TGCTCTGCCAATAC	-	1166	0.34	Training	Haem_ATL_74
CARD11	nonframeshift deletion	NM_032415	c.701_703del	p.234_235del	7	2979544	2979546	GGT	-	1022	0.316	Training	Haem_ATL_74
VAV1	nonsynonymous SNV	NM_005428	c.A77G	p.D26G	19	6772895	6772895	A	G	973	0.332	Training	Haem_ATL_74
PIK3CD	nonsynonymous SNV	NM_005026	c.T1823G	p.L608R	1	9781513	9781513	T	G	435	0.315	Training	Haem_ATL_75
RHOA	nonsynonymous SNV	NM_001664	c.G50T	p.G17V	3	49412973	49412973	C	A	690	0.287	Training	Haem_ATL_75
POT1	nonsynonymous SNV	NM_015450	c.G1792T	p.D598Y	7	124465306	124465306	C	A	785	0.364	Training	Haem_ATL_75
TP53	frameshift deletion	NM_000546	c.514delG	p.V172fs	17	7578416	7578416	C	-	648	0.611	Training	Haem_ATL_75
PDE7B	nonsynonymous SNV	NM_018945	c.A227C	p.Q76P	6	136468549	136468549	A	C	75	0.32	Training	Haem_ATL_76
HNRNPA2B1	stopgain	NM_002137	c.146delC	p.S49X	7	26237053	26237053	G	-	176	0.165	Training	Haem_ATL_76
FAS	frameshift deletion	NM_152872	c.660delT	p.T220fs	10	90773884	90773884	T	-	104	0.221	Training	Haem_ATL_76
TP53	nonsynonymous SNV	NM_000546	c.G646A	p.V216M	17	7578203	7578203	C	T	176	0.273	Training	Haem_ATL_76
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	647	0.527	Training	Haem_ATL_77
CSNK2B	stopgain	NM_001320	c.C544T	p.Q182X	6	31637272	31637272	C	T	614	0.497	Training	Haem_ATL_77
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	581	0.387	Training	Haem_ATL_77
CCR7	stopgain	NM_001838	c.G1064A	p.W355X	17	38711067	38711067	C	T	744	0.348	Training	Haem_ATL_77
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	983	0.501	Training	Haem_ATL_77
CD58	frameshift insertion	NM_001779	c.268_269insAGCC	p.L90fs	1	117087028	117087028	-	GGCT	483	0.47	Training	Haem_ATL_78
PTPRC	nonsynonymous SNV	NM_002838	c.A1774G	p.I592V	1	198697522	198697522	A	G	446	0.274	Training	Haem_ATL_78
IRF2BP2	frameshift deletion	NM_182972	c.1071_1075del	p.R357fs	1	234743572	234743576	GCTTC	-	230	0.117	Training	Haem_ATL_78
HLA-B	stopgain	NM_005514	c.G225A	p.W75X	6	31324583	31324583	C	T	175	0.389	Training	Haem_ATL_78
CSNK2B	splicing	NM_001282385	c.368-1G>A	NA	6	31637104	31637104	G	A	223	0.435	Training	Haem_ATL_78
HNRNPA2B1	splicing	NM_002137	c.964+2T>C	NA	7	26232869	26232869	A	G	370	0.035	Training	Haem_ATL_78
ZEB1	frameshift insertion	NM_030751	c.631dupT	p.A210fs	10	31799749	31799749	-	T	374	0.203	Training	Haem_ATL_78
RELA	stopgain	NM_021975	c.C985T	p.R329X	11	65423207	65423207	G	A	496	0.212	Training	Haem_ATL_78
PRKCB	nonframeshift deletion	NM_002738	c.83_85del	p.28_29del	16	23847579	23847581	AGA	-	556	0.347	Training	Haem_ATL_78
CSNK2A1	nonsynonymous SNV	NM_001895	c.C356A	p.T119K	20	479909	479909	G	T	396	0.369	Training	Haem_ATL_78
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	394	0.236	Training	Haem_ATL_78
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	479	0.219	Training	Haem_ATL_78
CARD11	nonsynonymous SNV	NM_032415	c.T2705G	p.F902C	7	2955005	2955005	A	C	377	0.408	Training	Haem_ATL_79
CCR4	frameshift insertion	NM_005508	c.1024_1025insCCCC	p.T342fs	3	32995938	32995938	-	CCCC	604	0.144	Training	Haem_ATL_80
TET2	stopgain	NM_017628	c.C973T	p.Q325X	4	106156072	106156072	C	T	535	0.228	Training	Haem_ATL_80
TET2	frameshift deletion	NM_017628	c.2798_2801del	p.Q933fs	4	106157897	106157900	AGGG	-	584	0.146	Training	Haem_ATL_80
CSNK2B	stopgain	NM_001320	c.564delC	p.Y188X	6	31637619	31637619	C	-	518	0.205	Training	Haem_ATL_80
GATA3	frameshift insertion	NM_002051	c.222_223insTACC	p.R74fs	10	8097840	8097840	-	TACC	663	0.157	Training	Haem_ATL_80
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	906	0.167	Training	Haem_ATL_81
HLA-B	nonsynonymous SNV	NM_005514	c.G1012A	p.G338S	6	31322884	31322884	C	T	485	0.115	Training	Haem_ATL_81
NFKBIA	splicing	NM_020529	c.337-1G>A	NA	14	35872567	35872567	C	T	266	0.049	Training	Haem_ATL_81
TP53	nonsynonymous SNV	NM_000546	c.G820T	p.V274F	17	7577118	7577118	C	A	592	0.091	Training	Haem_ATL_81
PLCG1	nonframeshift deletion	NM_002660	c.3502_3507del	p.1168_1169del	20	39802399	39802404	AGTGAC	-	1012	0.098	Training	Haem_ATL_81
CCR4	stopgain	NM_005508	c.C1041A	p.Y347X	3	32995955	32995955	C	A	1186	0.641	Training	Haem_ATL_82
TET2	stopgain	NM_017628	c.C1945T	p.Q649X	4	106157044	106157044	C	T	1187	0.612	Training	Haem_ATL_82
TET2	frameshift deletion	NM_001127208	c.4931_4947del	p.P1644fs	4	106196598	106196614	CATATCTGGGTTCCTAT	-	1741	0.225	Training	Haem_ATL_82
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	371	0.544	Training	Haem_ATL_82
CARD11	nonframeshift deletion	NM_032415	c.640_642del	p.214_214del	7	2983888	2983890	CTC	-	1292	0.244	Training	Haem_ATL_82
POT1	nonsynonymous SNV	NM_015450	c.G1891A	p.E631K	7	124464030	124464030	C	T	989	0.319	Training	Haem_ATL_82
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	827	0.042	Training	Haem_ATL_82
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	883	0.412	Training	Haem_ATL_82
TBL1XR1	nonframeshift deletion	NM_024665	c.971_973del	p.324_325del	3	176756175	176756177	AAG	-	1389	0.255	Training	Haem_ATL_83
STAT3	nonsynonymous SNV	NM_003150	c.A1919T	p.Y640F	17	40474482	40474482	T	A	960	0.329	Training	Haem_ATL_83
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	696	0.305	Training	Haem_ATL_83
PLCG1	nonsynonymous SNV	NM_002660	c.C2600G	p.P867R	20	39798116	39798116	C	G	644	0.307	Training	Haem_ATL_83
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	840	0.1	Training	Haem_ATL_84
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	355	0.087	Training	Haem_ATL_84
CSNK2B	stopgain	NM_001320	c.G517T	p.E173X	6	31637245	31637245	G	T	597	0.101	Training	Haem_ATL_84
CARD11	nonsynonymous SNV	NM_032415	c.C1853T	p.S618F	7	2963954	2963954	G	A	522	0.1	Training	Haem_ATL_84
CARD11	nonsynonymous SNV	NM_032415	c.G688A	p.D230N	7	2979559	2979559	C	T	642	0.089	Training	Haem_ATL_84
POT1	stopgain	NM_015450	c.C1294T	p.R432X	7	124481102	124481102	G	A	773	0.172	Training	Haem_ATL_84
IDH2	nonsynonymous SNV	NM_002168	c.G515A	p.R172K	15	90631838	90631838	C	T	567	0.097	Training	Haem_ATL_84
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	585	0.113	Training	Haem_ATL_84
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	759	0.109	Training	Haem_ATL_84
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	942	0.115	Training	Haem_ATL_85
TBL1XR1	nonsynonymous SNV	NM_024665	c.C1470G	p.C490W	3	176744209	176744209	G	C	872	0.258	Training	Haem_ATL_85
HLA-B	stopgain	NM_005514	c.C331T	p.Q111X	6	31324477	31324477	G	A	485	0.111	Training	Haem_ATL_85
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	251	0.482	Training	Haem_ATL_86
TET2	nonsynonymous SNV	NM_001127208	c.G4082A	p.G1361D	4	106190804	106190804	G	A	110	0.391	Training	Haem_ATL_86
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	106	0.387	Training	Haem_ATL_86
PLCG1	nonsynonymous SNV	NM_002660	c.G2606T	p.G869V	20	39798122	39798122	G	T	142	0.451	Training	Haem_ATL_86
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	114	0.439	Training	Haem_ATL_86
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	119	0.437	Training	Haem_ATL_87
STAT3	nonsynonymous SNV	NM_003150	c.A1919T	p.Y640F	17	40474482	40474482	T	A	62	0.435	Training	Haem_ATL_87
VAV1	nonsynonymous SNV	NM_005428	c.T530G	p.L177R	19	6822312	6822312	T	G	97	0.412	Training	Haem_ATL_87
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	89	0.416	Training	Haem_ATL_87
YTHDF2	frameshift deletion	NM_016258	c.295delT	p.F99fs	1	29069077	29069077	T	-	1099	0.311	Training	Haem_ATL_88
CCR4	frameshift insertion	NM_005508	c.983_984insCTGC	p.L328fs	3	32995897	32995897	-	CTGC	1299	0.178	Training	Haem_ATL_88
TBL1XR1	nonsynonymous SNV	NM_024665	c.C502A	p.H168N	3	176768324	176768324	G	T	664	0.288	Training	Haem_ATL_88
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	301	0.369	Training	Haem_ATL_89
TBL1XR1	nonsynonymous SNV	NM_024665	c.C793G	p.H265D	3	176765159	176765159	G	C	179	0.145	Training	Haem_ATL_89
CARD11	nonsynonymous SNV	NM_032415	c.T2705G	p.F902C	7	2955005	2955005	A	C	178	0.039	Training	Haem_ATL_89
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1290	0.303	Training	Haem_ATL_90
RHOA	nonsynonymous SNV	NM_001664	c.G50T	p.G17V	3	49412973	49412973	C	A	1390	0.187	Training	Haem_ATL_90
NOTCH1	stopgain	NM_017617	c.C7180T	p.Q2394X	9	139391011	139391011	G	A	573	0.04	Training	Haem_ATL_90
FAS	splicing	NM_000043	c.652-2A>C	NA	10	90773098	90773098	A	C	630	0.408	Training	Haem_ATL_90
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	850	0.031	Training	Haem_ATL_90
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	608	0.37	Training	Haem_ATL_90
YTHDF2	nonsynonymous SNV	NM_016258	c.G103C	p.E35Q	1	29064821	29064821	G	C	538	0.323	Training	Haem_ATL_92
IRF4	nonsynonymous SNV	NM_002460	c.C342G	p.S114R	6	394946	394946	C	G	399	0.449	Training	Haem_ATL_92
IRF4	nonsynonymous SNV	NM_002460	c.T347G	p.L116R	6	394951	394951	T	G	366	0.459	Training	Haem_ATL_92
CARD11	nonsynonymous SNV	NM_032415	c.G1159T	p.D387Y	7	2976853	2976853	C	A	205	0.317	Training	Haem_ATL_92
GATA3	frameshift insertion	NM_002051	c.702dupC	p.F234fs	10	8100727	8100727	-	C	547	0.223	Training	Haem_ATL_92
CCR7	frameshift deletion	NM_001838	c.1044_1047del	p.S348fs	17	38711084	38711087	CTGG	-	429	0.254	Training	Haem_ATL_92
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	240	0.279	Training	Haem_ATL_92
TET2	nonsynonymous SNV	NM_001127208	c.T3892C	p.C1298R	4	106180864	106180864	T	C	445	0.292	Training	Haem_ATL_93
TET2	stopgain	NM_001127208	c.G4219T	p.G1407X	4	106193757	106193757	G	T	561	0.251	Training	Haem_ATL_93
TET2	nonsynonymous SNV	NM_001127208	c.A5705C	p.Y1902S	4	106197372	106197372	A	C	562	0.034	Training	Haem_ATL_93
HLA-B	splicing	NM_005514	c.619+2->G	NA	6	31323942	31323942	-	C	44	0.159	Training	Haem_ATL_93
VAV1	nonsynonymous SNV	NM_005428	c.G1668C	p.E556D	19	6833596	6833596	G	C	282	0.309	Training	Haem_ATL_93
CD58	stopgain	NM_001779	c.C454T	p.R152X	1	117078761	117078761	G	A	441	0.515	Training	Haem_ATL_94
RHOA	nonsynonymous SNV	NM_001664	c.G50T	p.G17V	3	49412973	49412973	C	A	966	0.238	Training	Haem_ATL_94
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	582	0.375	Training	Haem_ATL_94
CARD11	nonsynonymous SNV	NM_032415	c.T1946C	p.F649S	7	2962962	2962962	A	G	284	0.338	Training	Haem_ATL_94
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	437	0.309	Training	Haem_ATL_94
RHOA	nonsynonymous SNV	NM_001664	c.G248A	p.C83Y	3	49405890	49405890	C	T	601	0.143	Training	Haem_ATL_95
CARD11	nonsynonymous SNV	NM_032415	c.G2203A	p.E735K	7	2962334	2962334	C	T	215	0.153	Training	Haem_ATL_95
FAS	nonsynonymous SNV	NM_000043	c.T5A	p.L2Q	10	90750638	90750638	T	A	311	0.186	Training	Haem_ATL_95

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	387	0.106	Training	Haem_ATL_95
PRKCB	nonsynonymous SNV	NM_002738	c.G1636A	p.E546K	16	24196802	24196802	G	A	344	0.134	Training	Haem_ATL_95
TNFAIP3	frameshift deletion	NM_006290	c.1494delC	p.C498fs	6	138200076	138200076	C	-	580	0.148	Training	Haem_ATL_96
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.C908T	p.P303L	7	26232927	26232927	G	A	290	0.114	Training	Haem_ATL_97
PLCG1	nonsynonymous SNV	NM_002660	c.G2120A	p.R707Q	20	39795235	39795235	G	A	136	0.037	Training	Haem_ATL_97
CCR4	frameshift insertion	NM_005508	c.967dupA	p.C322fs	3	32995880	32995880	-	A	1349	0.18	Training	Haem_ATL_98
TP53	nonsynonymous SNV	NM_000546	c.G733A	p.G245S	17	7577548	7577548	C	T	358	0.209	Training	Haem_ATL_98
STAT3	nonsynonymous SNV	NM_003150	c.A1982T	p.D661V	17	40474419	40474419	T	A	692	0.14	Training	Haem_ATL_98
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	908	0.466	Training	Haem_ATL_99
RHOA	nonsynonymous SNV	NM_001664	c.T46C	p.C16R	3	49412977	49412977	A	G	773	0.32	Training	Haem_ATL_99
TET2	stopgain	NM_017628	c.C2218T	p.Q740X	4	106157317	106157317	C	T	630	0.648	Training	Haem_ATL_99
FAS	frameshift deletion	NM_000043	c.696_741del	p.Y232fs	10	90773895	90773940	TATCACCACTATTGCTGGAGTCATGACACTAAGTCAAGTTAAAGGC	-	513	0.099	Training	Haem_ATL_99
CD58	frameshift deletion	NM_001779	c.88delT	p.S30fs	1	1.17E+08	1.17E+08	A	-	459	0.468	Validation	Haem_ATL_1
RHOA	nonsynonymous SNV	NM_001664	c.T46C	p.C16R	3	49412977	49412977	A	G	619	0.108	Validation	Haem_ATL_1
TBL1XR1	stopgain	NM_024665	c.C1291T	p.R431X	3	1.77E+08	1.77E+08	G	A	512	0.455	Validation	Haem_ATL_1
TP53	nonsynonymous SNV	NM_000546	c.T370G	p.C124G	17	7579317	7579317	A	C	152	0.382	Validation	Haem_ATL_1
VAV1	nonsynonymous SNV	NM_005428	c.G2383A	p.A795T	19	6854008	6854008	G	A	456	0.338	Validation	Haem_ATL_1
TET2	stopgain	NM_001127208	c.A4087T	p.K1363X	4	1.06E+08	1.06E+08	A	T	982	0.371	Validation	Haem_ATL_2
TET2	stopgain	NM_001127208	c.C4519T	p.Q1507X	4	1.06E+08	1.06E+08	C	T	297	0.175	Validation	Haem_ATL_2
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	611	0.504	Validation	Haem_ATL_2
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	959	0.377	Validation	Haem_ATL_2
TP53	nonsynonymous SNV	NM_000546	c.G733A	p.G245S	17	7577548	7577548	C	T	399	0.281	Validation	Haem_ATL_2
CCR4	frameshift insertion	NM_005508	c.966dupC	p.C322fs	3	32995879	32995879	-	C	1521	0.688	Validation	Haem_ATL_3
CSNK2A1	stopgain	NM_001895	c.C61T	p.R21X	20	489135	489135	G	A	488	0.344	Validation	Haem_ATL_3
GATA3	frameshift deletion	NM_002051	c.18_39del	p.D6fs	10	8097636	8097657	CCAGCCGCGCTGGGTGAGCCAC	-	271	0.218	Validation	Haem_ATL_4
GATA3	nonsynonymous SNV	NM_002051	c.C42G	p.H14Q	10	8097660	8097660	C	G	189	0.243	Validation	Haem_ATL_4
TP53	nonsynonymous SNV	NM_000546	c.G841C	p.D281H	17	7577097	7577097	C	G	233	0.592	Validation	Haem_ATL_4
S1PR1	frameshift insertion	NM_001400	c.499dupT	p.A166fs	1	1.02E+08	1.02E+08	-	T	908	0.379	Validation	Haem_ATL_6
CCR4	stopgain	NM_005508	c.C1034A	p.S345X	3	32995948	32995948	C	A	815	0.286	Validation	Haem_ATL_6
RHOA	nonsynonymous SNV	NM_001664	c.G481C	p.A161P	3	49397743	49397743	C	G	832	0.29	Validation	Haem_ATL_6
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	603	0.619	Validation	Haem_ATL_6
NOTCH1	stopgain	NM_017617	c.C7225T	p.Q2409X	9	1.39E+08	1.39E+08	G	A	227	0.912	Validation	Haem_ATL_6
CCR7	stopgain	NM_001838	c.G1064A	p.W355X	17	38711067	38711067	C	T	353	0.331	Validation	Haem_ATL_6
STAT3	nonsynonymous SNV	NM_003150	c.G2101T	p.A701S	17	40469240	40469240	C	A	344	0.384	Validation	Haem_ATL_6
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	389	0.44	Validation	Haem_ATL_6
PIK3CD	nonsynonymous SNV	NM_005026	c.A2254G	p.M752V	1	9782321	9782321	A	G	218	0.326	Validation	Haem_ATL_7
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	330	0.333	Validation	Haem_ATL_7
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	273	0.3	Validation	Haem_ATL_7
PLCG1	nonsynonymous SNV	NM_002660	c.A3506G	p.D1169G	20	39802403	39802403	A	G	282	0.039	Validation	Haem_ATL_7
TBL1XR1	nonsynonymous SNV	NM_024665	c.A42T	p.R14S	3	1.77E+08	1.77E+08	T	A	353	0.357	Validation	Haem_ATL_8
FAS	splicing	NM_000043	c.652-1G>T	NA	10	90773099	90773099	G	T	107	0.607	Validation	Haem_ATL_8
TP53	nonsynonymous SNV	NM_000546	c.C799G	p.R267G	17	7577139	7577139	G	C	275	0.636	Validation	Haem_ATL_8
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	812	0.096	Validation	Haem_ATL_8
IRF2BP2	nonsynonymous SNV	NM_182972	c.C274G	p.L92V	1	2.35E+08	2.35E+08	G	C	64	0.328	Validation	Haem_ATL_9
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	1221	0.573	Validation	Haem_ATL_9
IRF4	nonsynonymous SNV	NM_002460	c.C342A	p.S114R	6	394946	394946	C	A	543	0.18	Validation	Haem_ATL_9
HLA-B	stopgain	NM_005514	c.G723A	p.W241X	6	31323266	31323266	C	T	264	0.436	Validation	Haem_ATL_9
PRKCB	nonsynonymous SNV	NM_002738	c.G1126A	p.D376N	16	24166065	24166065	G	A	575	0.315	Validation	Haem_ATL_9
VAV1	nonsynonymous SNV	NM_005428	c.G469A	p.E157K	19	6822251	6822251	G	A	270	0.507	Validation	Haem_ATL_9
EP300	splicing	NA	NA	NA	22	41551118	41551121	GTAA	-	1083	0.237	Validation	Haem_ATL_9
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	1013	0.554	Validation	Haem_ATL_10
GATA3	nonsynonymous SNV	NM_002051	c.G862A	p.G288R	10	8106042	8106042	G	A	628	0.398	Validation	Haem_ATL_10
CCR7	stopgain	NM_001838	c.G1065A	p.W355X	17	38711066	38711066	C	T	501	0.365	Validation	Haem_ATL_10
PLCG1	nonsynonymous SNV	NM_002660	c.T3499G	p.F1167V	20	39802396	39802396	T	G	642	0.329	Validation	Haem_ATL_10
TBL1XR1	nonsynonymous SNV	NM_024665	c.T1341G	p.S447R	3	1.77E+08	1.77E+08	A	C	497	0.928	Validation	Haem_ATL_11
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	1628	0.225	Validation	Haem_ATL_12
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1328T	p.E443V	3	1.77E+08	1.77E+08	T	A	956	0.231	Validation	Haem_ATL_12
CARD11	nonsynonymous SNV	NM_032415	c.C1952G	p.P651R	7	2962956	2962956	G	C	664	0.297	Validation	Haem_ATL_12
CARD11	nonsynonymous SNV	NM_032415	c.A1082G	p.Y361C	7	2977602	2977602	T	C	877	0.273	Validation	Haem_ATL_12
NFKBIA	nonsynonymous SNV	NM_020529	c.C193G	p.P65A	14	35873658	35873658	G	C	610	0.134	Validation	Haem_ATL_12
PLCG1	nonframeshift deletion	NM_002660	c.3509_3511del	p.1170_1171del	20	39802406	39802408	AGA	-	1470	0.121	Validation	Haem_ATL_12
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1492	0.186	Validation	Haem_ATL_13
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	1112	0.18	Validation	Haem_ATL_13
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.C907A	p.P303T	7	26232928	26232928	G	T	1494	0.17	Validation	Haem_ATL_13
PLCG1	nonsynonymous SNV	NM_002660	c.C2617T	p.R873W	20	39798133	39798133	C	T	992	0.163	Validation	Haem_ATL_13
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	1493	0.166	Validation	Haem_ATL_13
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	1151	0.279	Validation	Haem_ATL_14
CSNK2B	stopgain	NM_001320	c.G517T	p.E173X	6	31637245	31637245	G	T	1126	0.153	Validation	Haem_ATL_14
CD58	stopgain	NM_001779	c.C471G	p.Y157X	1	1.17E+08	1.17E+08	G	C	918	0.27	Validation	Haem_ATL_15
CDKN2A	stopgain	NM_000077	c.C238T	p.R80X	9	21971120	21971120	G	A	416	0.466	Validation	Haem_ATL_15
GATA3	stopgain	NM_002051	c.C166T	p.Q56X	10	8097784	8097784	C	T	987	0.305	Validation	Haem_ATL_15
FAS	frameshift deletion	NM_000043	c.608_630del	p.R203fs	10	90771795	90771817	GAAAGGAAAACCAAGGTTCTCAT	-	1064	0.372	Validation	Haem_ATL_15
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	974	0.309	Validation	Haem_ATL_15
CCR4	nonframeshift deletion	NM_005508	c.1043_1060del	p.348_354del	3	32995957	32995974	CGCAGTCCACCATGGATC	-	2461	0.295	Validation	Haem_ATL_16
TET2	frameshift deletion	NM_001127208	c.4863_4870del	p.L1621fs	4	1.06E+08	1.06E+08	TTTGAATC	-	2335	0.204	Validation	Haem_ATL_16
GATA3	frameshift insertion	NM_002051	c.305dupC	p.A102fs	10	8100330	8100330	-	C	1720	0.251	Validation	Haem_ATL_16
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1094	0.266	Validation	Haem_ATL_16
PLCG1	nonsynonymous SNV	NM_002660	c.G141C	p.E47D	20	39766422	39766422	G	C	777	0.248	Validation	Haem_ATL_16
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	778	0.247	Validation	Haem_ATL_16
PLCG1	nonsynonymous SNV	NM_002660	c.T1525G	p.Y509D	20	39794105	39794105	T	G	1128	0.277	Validation	Haem_ATL_16
TP53	nonsynonymous SNV	NM_000546	c.G404A	p.C135Y	17	7578526	7578526	C	T	187	0.759	Validation	Haem_ATL_17
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	237	0.468	Validation	Haem_ATL_17
PLCG1	nonsynonymous SNV	NM_002660	c.A3047T	p.Q1016L	20	39801202	39801202	A	T	447	0.125	Validation	Haem_ATL_17
TBL1XR1	nonsynonymous SNV	NM_024665	c.C1499T	p.A500V	3	1.77E+08	1.77E+08	G	A	462	0.188	Validation	Haem_ATL_18
TBL1XR1	stopgain	NM_024665	c.1337dupA	p.Y446_S447delinsX	3	1.77E+08	1.77E+08	-	T	518	0.243	Validation	Haem_ATL_18
TBL1XR1	nonsynonymous SNV	NM_024665	c.C563A	p.S188Y	3	1.77E+08	1.77E+08	G	T	431	0.216	Validation	Haem_ATL_18
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	426	0.232	Validation	Haem_ATL_18
VAV1	nonsynonymous SNV	NM_005428	c.C1195T	p.H399Y	19	6828841	6828841	C	T	283	0.265	Validation	Haem_ATL_18
VAV1	nonsynonymous SNV	NM_005428	c.G2393A	p.R798Q	19	6854018	6854018	G	A	243	0.255	Validation	Haem_ATL_18
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	218	0.22	Validation	Haem_ATL_18
PLCG1	nonsynonymous SNV	NM_002660	c.G2606C	p.G869A	20	39798122	39798122	G	C	310	0.045	Validation	Haem_ATL_18
CD58	frameshift deletion	NM_001779	c.641delA	p.H214fs	1	1.17E+08	1.17E+08	T	-	1634	0.078	Validation	Haem_ATL_19
TBL1XR1	nonsynonymous SNV	NM_024665	c.C1103T	p.S368F	3	1.77E+08	1.77E+08	G	A	1716	0.101	Validation	Haem_ATL_19
HLA-B	stopgain	NM_005514	c.C843G	p.Y281X	6	31323146	31323146	G	C	1624	0.105	Validation	Haem_ATL_19
HNRNPA2B1	nonsynonymous SNV	NM_002137	c.G533C	p.R178T	7	26236221	26236221	C	G	1945	0.101	Validation	Haem_ATL_19
GATA3	frameshift deletion	NM_002051	c.1057delC	p.P353fs	10	8115711	8115711	C	-	1412	0.089	Validation	Haem_ATL_19
RELA	nonsynonymous SNV	NM_021975	c.G115C	p.E39Q	11	65429479	65429479	C	G	1102	0.125	Validation	Haem_ATL_19
PRKCB	nonsynonymous SNV	NM_002738	c.G1457A	p.G486D	16	24192173	24192173	G	A	1725	0.107	Validation	Haem_ATL_19
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	1793	0.075	Validation	Haem_ATL_19
EP300	stopgain	NM_001429	c.C382T	p.Q128X	22	41513478	41513478	C	T	2039	0.198	Validation	Haem_ATL_19
IRF4	nonsynonymous SNV	NM_002460	c.T347G	p.L116R	6	394951	394951	T	G	443	0.142	Validation	Haem_ATL_20
CARD11	nonsynonymous SNV	NM_032415	c.G2203A	p.E735K	7	2962334	2962334	C	T	1365	0.073	Validation	Haem_ATL_20
PRKCB	nonsynonymous SNV	NM_002738	c.G1888T	p.D630Y	16	24226003	24226003	G	T	69	0.13	Validation	Haem_ATL_20
PLCG1	nonframeshift deletion	NM_002660	c.3508_3513del	p.1170_1171del	20	39802405	39802410	CAGAAT	-	652	0.052	Validation	Haem_ATL_20
CCR4	frameshift deletion	NM_005508	c.968_972del	p.R323fs	3	32995882	32995886	GGGGC	-	1856	0.408	Validation	Haem_ATL_21
RHOA	nonsynonymous SNV	NM_001664	c.A359G	p.D120G	3	49399978	49399978	T	C	1350	0.056	Validation	Haem_ATL_21
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	1094	0.045	Validation	Haem_ATL_21
NOTCH1	stopgain	NM_017617	c.C7459T	p.Q2487X	9	1.39E+08	1.39E+08	G	A	895	0.05	Validation	Haem_ATL_21
CCR7	stopgain	NM_001838	c.C1045T	p.Q349X	17	38711086	38711086	G	A	1435	0.067	Validation	Haem_ATL_21
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1764	0.377	Validation	Haem_ATL_24
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	975	0.417	Validation	Haem_ATL_24
IDH2	nonsynonymous SNV	NM_002168	c.A514G	p.R172G	15	90631839	90631839	T	C	1221	0.164	Validation	Haem_ATL_24
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1010	0.095	Validation	Haem_ATL_24
CCR4	frameshift insertion	NM_005508	c.967dupA	p.C322fs	3	32995880	32995880	-	A	1368	0.402	Validation	Haem_ATL_26
CARD11	nonsynonymous SNV	NM_032415	c.A2677T	p.S893C	7	2956950	2956950	T	A	634	0.462	Validation	Haem_ATL_26
CARD11	nonsynonymous SNV	NM_032415	c.G1201A	p.D401N	7	2976811	2976811	C	T	946	0.467	Validation	Haem_ATL_26
NOTCH1	frameshift deletion	NM_017617	c.7222delC	p.L2408fs	9	1.39E+08	1.39E+08	G	-	545	0.422	Validation	Haem_ATL_26
CCR7	stopgain	NM_001838	c.C1051T	p.Q351X	17	38711080	38711080	G	A	919	0.4	Validation	Haem_ATL_26
STAT3	nonsynonymous SNV	NM_003150	c.A1919T	p.Y640F	17	40474482	40474482	T	A	1000	0.478	Validation	Haem_ATL_26
CCR4	frameshift deletion	NM_005508	c.1035_1039del	p.S345fs	3	32995949	32995953	ATCTT	-	1321	0.379	Validation	Haem_ATL_27
CSNK2B	stopgain	NM_001320	c.G517T	p.E173X	6	31637245	31637245	G	T	983	0.412	Validation	Haem_ATL_27
CARD11	nonsynonymous SNV	NM_032415	c.C1071A	p.D357E	7	2977613	2977613	G	T	914	0.048	Validation	Haem_ATL_27
GATA3	splicing	NM_002051	c.1048-1G>C	NA	10	8115701	8115701	G	C	739	0.398	Validation	Haem_ATL_27
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	1012	0.418	Validation	Haem_ATL_27
CCR4	frameshift deletion	NM_005508	c.954_961del	p.L318fs	3	32995868	32995875	CTTCAAAA	-	1544	0.35	Validation	Haem_ATL_28
CCR4	frameshift insertion	NM_005508	c.989dupA	p.Q330fs	3	32995902	32995902	-	A	1803	0.136	Validation	Haem_ATL_29
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	877	0.147	Validation	Haem_ATL_29
TP53	splicing	NM_000546	c.376-1G>C	NA	17	7578555	7578555	C	G	755	0.294	Validation	Haem_ATL_29
CD28	nonsynonymous SNV	NM_006139	c.C372G	p.D124E	2	2.05E+08	2.05E+08	C	G	1610	0.104	Validation	Haem_ATL_30
CCR4	stopgain	NM_005508	c.C988T	p.Q330X	3	32995902	32995902	C	T	1830	0.087	Validation	Haem_ATL_30
TBL1XR1	nonsynonymous SNV	NM_024665	c.T1059A	p.N353K	3	1.77E+08	1.77E+08	A	T	1266	0.025	Validation	Haem_ATL_30
NOTCH1	stopgain	NM_017617	c.C7246T	p.Q2416X	9	1.39E+08	1.39E+08	G	A	438	0.126	Validation	Haem_ATL_30

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
TP53	nonsynonymous SNV	NM_000546	c.G814T	p.V272L	17	7577124	7577124	C	A	513	0.037	Validation	Haem_ATL_30
STAT3	nonsynonymous SNV	NM_003150	c.G1852C	p.G618R	17	40475058	40475058	C	G	964	0.525	Validation	Haem_ATL_30
VAV1	nonsynonymous SNV	NM_005428	c.A524T	p.E175V	19	6822306	6822306	A	T	441	0.764	Validation	Haem_ATL_30
VAV1	nonframeshift deletion	NM_005428	c.2335_2352del	p.779_784del	19	6853960	6853977	GGAAGCACAAAGTATTTT	-	1077	0.605	Validation	Haem_ATL_30
IRF4	nonsynonymous SNV	NM_002460	c.G196A	p.E66K	6	393348	393348	G	A	726	0.186	Validation	Haem_ATL_31
ATXN1	stopgain	NM_000332	c.C1973A	p.S658X	6	16307035	16307035	G	T	751	0.26	Validation	Haem_ATL_31
HLA-B	stopgain	NM_005514	c.G225A	p.W75X	6	31324583	31324583	C	T	697	0.211	Validation	Haem_ATL_31
B2M	stopgain	NM_004048	c.T20A	p.L7X	15	45003764	45003764	T	A	664	0.191	Validation	Haem_ATL_31
PRKCB	nonsynonymous SNV	NM_002738	c.G65A	p.R22H	16	23847561	23847561	G	A	635	0.217	Validation	Haem_ATL_31
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1413	0.078	Validation	Haem_ATL_32
GATA3	frameshift deletion	NM_002051	c.81delC	p.H27fs	10	8097699	8097699	C	-	790	0.039	Validation	Haem_ATL_32
IRF2BP2	nonsynonymous SNV	NM_182972	c.G116T	p.G39V	1	2.35E+08	2.35E+08	C	A	516	0.12	Validation	Haem_ATL_33
ZFP36L2	frameshift insertion	NM_006887	c.1395dupC	p.S466fs	2	43451547	43451547	-	G	255	0.212	Validation	Haem_ATL_33
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	1707	0.299	Validation	Haem_ATL_33
RHOA	nonsynonymous SNV	NM_001664	c.G50T	p.G17V	3	49412973	49412973	C	A	1239	0.165	Validation	Haem_ATL_33
HLA-B	nonsynonymous SNV	NM_005514	c.G3T	p.M1I	6	31324933	31324933	C	A	448	0.201	Validation	Haem_ATL_33
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	872	0.053	Validation	Haem_ATL_33
STAT3	nonsynonymous SNV	NM_003150	c.G641A	p.R214Q	17	40489785	40489785	C	T	864	0.109	Validation	Haem_ATL_33
VAV1	nonsynonymous SNV	NM_005428	c.A1211G	p.K404R	19	6828857	6828857	A	G	1049	0.203	Validation	Haem_ATL_33
EP300	stopgain	NM_001429	c.C604T	p.R202X	22	41513700	41513700	C	T	1056	0.221	Validation	Haem_ATL_33
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	1102	0.263	Validation	Haem_ATL_34
TBL1XR1	nonsynonymous SNV	NM_024665	c.A920C	p.H307P	3	1.77E+08	1.77E+08	T	G	700	0.297	Validation	Haem_ATL_34
CSNK2B	nonsynonymous SNV	NM_001320	c.T102G	p.F34L	6	31635674	31635674	T	G	948	0.138	Validation	Haem_ATL_34
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	1015	0.23	Validation	Haem_ATL_34
VAV1	nonsynonymous SNV	NM_005428	c.A1196T	p.H399L	19	6828842	6828842	A	T	938	0.493	Validation	Haem_ATL_34
CSNK1A1	nonsynonymous SNV	NM_001892	c.G85A	p.G29R	5	1.49E+08	1.49E+08	C	T	770	0.188	Validation	Haem_ATL_35
STAT3	nonsynonymous SNV	NM_003150	c.G1852C	p.G618R	17	40475058	40475058	C	G	715	0.19	Validation	Haem_ATL_35
CARD11	nonsynonymous SNV	NM_032415	c.G688A	p.D230N	7	2979559	2979559	C	T	1115	0.38	Validation	Haem_ATL_37
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	649	0.039	Validation	Haem_ATL_38
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1290	0.185	Validation	Haem_ATL_39
FYN	nonsynonymous SNV	NM_002037	c.C526T	p.R176C	6	1.12E+08	1.12E+08	G	A	961	0.085	Validation	Haem_ATL_39
NFKBIA	stopgain	NM_020529	c.C130T	p.Q44X	14	35873721	35873721	G	A	832	0.232	Validation	Haem_ATL_39
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	646	0.257	Validation	Haem_ATL_39
PLCG1	nonsynonymous SNV	NM_002660	c.G2258C	p.R753P	20	39795456	39795456	G	C	981	0.14	Validation	Haem_ATL_39
CCR4	frameshift insertion	NM_005508	c.967dupA	p.C322fs	3	32995880	32995880	-	A	1118	0.457	Validation	Haem_ATL_40
IRF4	nonsynonymous SNV	NM_002460	c.A1169C	p.E390A	6	405087	405087	A	C	313	0.374	Validation	Haem_ATL_40
HLA-B	stopgain	NM_005514	c.C358T	p.Q120X	6	31324205	31324205	G	A	31	0.548	Validation	Haem_ATL_40
GPR183	frameshift insertion	NM_004951	c.795dupT	p.Q266fs	13	99947604	99947604	-	A	440	0.455	Validation	Haem_ATL_40
TP53	nonsynonymous SNV	NM_000546	c.G524A	p.R175H	17	7578406	7578406	C	T	87	0.575	Validation	Haem_ATL_40
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	214	0.079	Validation	Haem_ATL_40
PLCG1	nonsynonymous SNV	NM_002660	c.G2605A	p.G869R	20	39798121	39798121	G	A	246	0.033	Validation	Haem_ATL_40
KDM6A	stopgain	NM_021140	c.C2128T	p.Q710X	X	44929028	44929028	C	T	131	0.466	Validation	Haem_ATL_40
GATA3	splicing	NM_002051	c.241+1G>A	NA	10	8097860	8097860	G	A	72	0.736	Validation	Haem_ATL_41
IDH2	nonsynonymous SNV	NM_002168	c.G515A	p.R172K	15	90631838	90631838	C	T	155	0.439	Validation	Haem_ATL_41
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	324	0.435	Validation	Haem_ATL_41
NOTCH1	frameshift deletion	NM_017617	c.7541_7542del	p.P2514fs	9	1.39E+08	1.39E+08	AG	-	264	0.163	Validation	Haem_ATL_42
PRKCB	nonsynonymous SNV	NM_002738	c.G1046A	p.G349E	16	24135283	24135283	G	A	176	0.301	Validation	Haem_ATL_42
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	157	0.038	Validation	Haem_ATL_42
PLCG1	nonsynonymous SNV	NM_002660	c.A430G	p.T144A	20	39788569	39788569	A	G	168	0.167	Validation	Haem_ATL_42
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	123	0.301	Validation	Haem_ATL_42
TBL1XR1	nonsynonymous SNV	NM_024665	c.A860T	p.D287V	3	1.77E+08	1.77E+08	T	A	296	0.22	Validation	Haem_ATL_43
CARD11	nonsynonymous SNV	NM_032415	c.G1159T	p.D387Y	7	2976853	2976853	C	A	352	0.457	Validation	Haem_ATL_43
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	605	0.357	Validation	Haem_ATL_44
IRF4	nonsynonymous SNV	NM_002460	c.C70T	p.L24F	6	393222	393222	C	T	265	0.2	Validation	Haem_ATL_44
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	365	0.682	Validation	Haem_ATL_44
CD58	frameshift deletion	NM_001779	c.356delA	p.Y119fs	1	1.17E+08	1.17E+08	T	-	103	0.117	Validation	Haem_ATL_45
CCR4	frameshift insertion	NM_005508	c.1024_1025insCCCC	p.T342fs	3	32995938	32995938	-	CCCC	1261	0.377	Validation	Haem_ATL_45
TBL1XR1	nonsynonymous SNV	NM_024665	c.A794C	p.H265P	3	1.77E+08	1.77E+08	T	G	354	0.946	Validation	Haem_ATL_45
TET2	frameshift deletion	NM_001127208	c.3951_3952del	p.K1317fs	4	1.06E+08	1.06E+08	AG	-	517	0.422	Validation	Haem_ATL_45
TET2	stopgain	NM_001127208	c.C4210T	p.R1404X	4	1.06E+08	1.06E+08	C	T	481	0.449	Validation	Haem_ATL_45
HLA-B	frameshift insertion	NM_005514	c.626dupC	p.P209fs	6	31323362	31323362	-	G	257	0.724	Validation	Haem_ATL_45
PDE7B	splicing	NM_018945	c.580-2A>G	NA	6	1.36E+08	1.36E+08	A	G	186	0.457	Validation	Haem_ATL_45
ZEB1	stopgain	NM_030751	c.C973T	p.R325X	10	31809236	31809236	C	T	562	0.427	Validation	Haem_ATL_45
FAS	nonsynonymous SNV	NM_000043	c.A775G	p.I259V	10	90773974	90773974	A	G	472	0.479	Validation	Haem_ATL_45
FAS	nonsynonymous SNV	NM_000043	c.C795A	p.D265E	10	90773994	90773994	C	A	450	0.464	Validation	Haem_ATL_45
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	891	0.444	Validation	Haem_ATL_45
VAV1	nonsynonymous SNV	NM_005428	c.C1492A	p.Q498K	19	6832195	6832195	C	A	287	0.178	Validation	Haem_ATL_45
FAS	nonsynonymous SNV	NM_000043	c.A788C	p.K263T	10	90773987	90773987	A	C	295	0.349	Validation	Haem_ATL_47
TP53	stopgain	NM_000546	c.A358T	p.K120X	17	7579329	7579329	T	A	74	0.703	Validation	Haem_ATL_47
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	426	0.481	Validation	Haem_ATL_48
HLA-B	frameshift insertion	NM_005514	c.338_339insT	p.E113fs	6	31324469	31324469	-	A	73	0.849	Validation	Haem_ATL_48
HLA-B	nonsynonymous SNV	NM_005514	c.G149A	p.G50D	6	31324659	31324659	C	T	113	0.735	Validation	Haem_ATL_48
CARD11	nonsynonymous SNV	NM_032415	c.C335T	p.T112I	7	2985476	2985476	G	A	796	0.648	Validation	Haem_ATL_48
PRKCB	nonsynonymous SNV	NM_002738	c.A1280G	p.D427G	16	24183631	24183631	A	G	272	0.382	Validation	Haem_ATL_48
CD58	nonframeshift deletion	NM_001779	c.391_402del	p.131_134del	1	1.17E+08	1.17E+08	AGTCAATGCACA	-	365	0.345	Validation	Haem_ATL_49
IRF2BP2	nonsynonymous SNV	NM_182972	c.G715A	p.A239T	1	2.35E+08	2.35E+08	C	T	84	0.345	Validation	Haem_ATL_49
IRF2BP2	nonsynonymous SNV	NM_182972	c.G653C	p.G218A	1	2.35E+08	2.35E+08	C	G	49	0.265	Validation	Haem_ATL_49
CCR4	stopgain	NM_005508	c.C987A	p.C329X	3	32995901	32995901	C	A	700	0.301	Validation	Haem_ATL_49
TBL1XR1	nonframeshift deletion	NM_024665	c.865_873del	p.289_291del	3	1.77E+08	1.77E+08	AATTGTAGTCTGAGATTAAAAGG	-	867	0.125	Validation	Haem_ATL_49
TBL1XR1	splicing	NM_024665	c.767-1G>A	NA	3	1.77E+08	1.77E+08	C	T	333	0.511	Validation	Haem_ATL_49
CSNK1A1	nonsynonymous SNV	NM_001892	c.G292A	p.E98K	5	1.49E+08	1.49E+08	C	T	480	0.342	Validation	Haem_ATL_49
HLA-B	stopgain	NM_005514	c.C535T	p.Q179X	6	31324028	31324028	G	A	129	0.372	Validation	Haem_ATL_49
HLA-B	frameshift deletion	NM_005514	c.265_266del	p.Q89fs	6	31324542	31324543	TG	-	330	0.424	Validation	Haem_ATL_49
FAS	nonsynonymous SNV	NM_000043	c.T776C	p.I259T	10	90773975	90773975	T	C	429	0.324	Validation	Haem_ATL_49
CCR4	frameshift insertion	NM_005508	c.989dupA	p.Q330fs	3	32995902	32995902	-	A	954	0.172	Validation	Haem_ATL_50
TBL1XR1	nonsynonymous SNV	NM_024665	c.C1470G	p.C490W	3	1.77E+08	1.77E+08	G	C	679	0.032	Validation	Haem_ATL_50
TBL1XR1	nonsynonymous SNV	NM_024665	c.G931C	p.A311P	3	1.77E+08	1.77E+08	C	G	352	0.122	Validation	Haem_ATL_50
CSNK1A1	nonframeshift deletion	NM_001892	c.82_84del	p.28_28del	5	1.49E+08	1.49E+08	GAA	-	656	0.172	Validation	Haem_ATL_50
ATXN1	stopgain	NM_000332	c.C727T	p.Q243X	6	16327815	16327815	G	A	345	0.145	Validation	Haem_ATL_50
CARD11	nonsynonymous SNV	NM_032415	c.A1235T	p.E412V	7	2976777	2976777	T	A	395	0.197	Validation	Haem_ATL_50
CARD11	nonsynonymous SNV	NM_032415	c.A1160T	p.D387V	7	2976852	2976852	T	A	246	0.203	Validation	Haem_ATL_50
PLCG1	nonsynonymous SNV	NM_002660	c.A2248G	p.M750V	20	39795446	39795446	A	G	351	0.217	Validation	Haem_ATL_50
KDM6A	stopgain	NM_021140	c.C997T	p.Q333X	X	44918514	44918514	C	T	108	0.407	Validation	Haem_ATL_50
IRF2BP2	nonsynonymous SNV	NM_182972	c.G1060C	p.A354P	1	2.35E+08	2.35E+08	C	G	107	0.43	Validation	Haem_ATL_51
IRF2BP2	stopgain	NM_182972	c.C289T	p.Q97X	1	2.35E+08	2.35E+08	G	A	38	0.342	Validation	Haem_ATL_51
ZFP36L2	stopgain	NM_006887	c.C1201T	p.Q401X	2	43451742	43451742	G	A	10	0.5	Validation	Haem_ATL_51
ZFP36L2	nonsynonymous SNV	NM_006887	c.C1105T	p.L369F	2	43451838	43451838	G	A	38	0.342	Validation	Haem_ATL_51
ZFP36L2	nonsynonymous SNV	NM_006887	c.G51C	p.K17N	2	43453404	43453404	C	G	119	0.353	Validation	Haem_ATL_51
CD28	nonsynonymous SNV	NM_006139	c.T151A	p.F51I	2	2.05E+08	2.05E+08	T	A	567	0.517	Validation	Haem_ATL_51
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	463	0.324	Validation	Haem_ATL_51
TBL1XR1	stopgain	NM_024665	c.G699A	p.W233X	3	1.77E+08	1.77E+08	C	T	185	0.524	Validation	Haem_ATL_51
HLA-B	stopgain	NM_005514	c.G610T	p.E204X	6	31323953	31323953	C	A	10	0.6	Validation	Haem_ATL_51
NOTCH1	frameshift deletion	NM_017617	c.7541_7542del	p.P2514fs	9	1.39E+08	1.39E+08	AG	-	631	0.304	Validation	Haem_ATL_51
PTPRC	nonsynonymous SNV	NM_002838	c.G3633C	p.M1211I	1	1.99E+08	1.99E+08	G	C	1116	0.314	Validation	Haem_ATL_52
RHOA	nonsynonymous SNV	NM_001664	c.G358A	p.D120N	3	49399979	49399979	C	T	524	0.258	Validation	Haem_ATL_52
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	931	0.542	Validation	Haem_ATL_52
HLA-B	nonsynonymous SNV	NM_005514	c.G751A	p.D251N	6	31323238	31323238	C	T	486	0.082	Validation	Haem_ATL_52
HLA-B	stopgain	NM_005514	c.G225A	p.W75X	6	31324583	31324583	C	T	219	0.484	Validation	Haem_ATL_52
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	452	0.723	Validation	Haem_ATL_52
PRKCB	nonsynonymous SNV	NM_002738	c.G65A	p.R22H	16	23847561	23847561	G	A	657	0.09	Validation	Haem_ATL_52
PLCG1	nonsynonymous SNV	NM_002660	c.G2120A	p.R707Q	20	39795235	39795235	G	A	365	0.342	Validation	Haem_ATL_52
PLCG1	nonsynonymous SNV	NM_002660	c.A2197C	p.S733R	20	39795395	39795395	A	C	537	0.298	Validation	Haem_ATL_52
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	845	0.164	Validation	Haem_ATL_53
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1106G	p.D369G	3	1.77E+08	1.77E+08	T	C	679	0.334	Validation	Haem_ATL_53
TET2	nonsynonymous SNV	NM_001127208	c.G4859A	p.G1620E	4	1.06E+08	1.06E+08	G	A	675	0.172	Validation	Haem_ATL_53
NOTCH1	stopgain	NM_017617	c.C7459T	p.Q2487X	9	1.39E+08	1.39E+08	G	A	257	0.035	Validation	Haem_ATL_53
FAS	frameshift deletion	NM_000043	c.347delA	p.E116fs	10	90768658	90768658	A	-	1145	0.173	Validation	Haem_ATL_53
FAS	nonsynonymous SNV	NM_000043	c.T776C	p.I259T	10	90773975	90773975	T	C	638	0.171	Validation	Haem_ATL_53
RELA	nonsynonymous SNV	NM_021975	c.G115C	p.E39Q	11	65429479	65429479	C	G	320	0.163	Validation	Haem_ATL_53
PRKCB	nonsynonymous SNV	NM_002738	c.G1888A	p.D630N	16	24226003	24226003	G	A	880	0.053	Validation	Haem_ATL_53
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	341	0.208	Validation	Haem_ATL_53
PLCG1	nonsynonymous SNV	NM_002660	c.C1559T	p.S520F	20	39794139	39794139	C	T	324	0.157	Validation	Haem_ATL_53
IRF2BP2	nonsynonymous SNV	NM_182972	c.C1381A	p.P461T	1	2.35E+08	2.35E+08	G	T	538	0.229	Validation	Haem_ATL_54
RHOA	nonsynonymous SNV	NM_001664	c.G248A	p.C83Y	3	49405890	49405890	C	T	536	0.106	Validation	Haem_ATL_54
NOTCH1	stopgain	NM_017617	c.C7375T	p.Q2459X	9	1.39E+08	1.39E+08	G	A	185	0.286	Validation	Haem_ATL_54
GATA3	frameshift deletion	NM_002051	c.525delG	p.S175fs	10	8100551	8100551	G	-	976	0.245	Validation	Haem_ATL_54
NFKBIA	stopgain	NM_020529	c.C202T	p.Q68X	14	35873649	35873649	G	A	422	0.242	Validation	Haem_ATL_54
CD58	stopgain	NM_001779	c.C94T	p.Q32X	1	1.17E+08	1.17E+08	G	A	423	0.371	Validation	Haem_ATL_55
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	906	0.51	Validation	Haem_ATL_55
HLA-B	stopgain	NM_005514	c.G722A	p.W241X	6	31323267	31323267	C	T	579	0.028	Validation	Haem_ATL_55
PRKCB	nonsynonymous SNV	NM_002738	c.G1597A	p.E533K	16	24196495	24196495	G	A	529	0.278	Validation	Haem_ATL_55
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	586	0.481	Validation	Haem_ATL_55

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
PLCG1	nonsynonymous SNV	NM_002660	c.G2120A	p.R707Q	20	39795235	39795235	G	A	451	0.497	Validation	Haem_ATL_55
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	898	0.35	Validation	Haem_ATL_56
CARD11	nonsynonymous SNV	NM_032415	c.T2705G	p.F902C	7	2955005	2955005	A	C	354	0.703	Validation	Haem_ATL_56
CDKN2A	stopgain	NM_000077	c.C238T	p.R80X	9	21971120	21971120	G	A	1319	0.847	Validation	Haem_ATL_56
ZEB1	stopgain	NM_030751	c.C2227T	p.Q743X	10	31810490	31810490	C	T	824	0.283	Validation	Haem_ATL_56
CCR7	stopgain	NM_001838	c.C1060T	p.Q354X	17	38711071	38711071	G	A	494	0.316	Validation	Haem_ATL_56
PLCG1	nonframeshift deletion	NM_002660	c.3502_3507del	p.1168_1169del	20	39802399	39802404	AGTGAC	-	1009	0.571	Validation	Haem_ATL_56
YTHDF2	frameshift deletion	NM_016258	c.1443_1444del	p.T481fs	1	29070225	29070226	AT	-	1406	0.36	Validation	Haem_ATL_57
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	580	0.409	Validation	Haem_ATL_57
TP53	nonsynonymous SNV	NM_000546	c.G856A	p.E286K	17	7577082	7577082	C	T	423	0.624	Validation	Haem_ATL_57
CARD11	nonsynonymous SNV	NM_032415	c.T1852G	p.S618A	7	2963955	2963955	A	C	360	0.156	Validation	Haem_ATL_58
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	483	0.07	Validation	Haem_ATL_58
PRKCB	nonsynonymous SNV	NM_002738	c.G1408C	p.D470H	16	24192124	24192124	G	C	598	0.102	Validation	Haem_ATL_58
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	868	0.282	Validation	Haem_ATL_58
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	613	0.233	Validation	Haem_ATL_58
CBLB	stopgain	NM_170662	c.C112T	p.Q38X	3	1.06E+08	1.06E+08	G	A	949	0.413	Validation	Haem_ATL_59
TBL1XR1	stopgain	NM_024665	c.421delA	p.I141X	3	1.77E+08	1.77E+08	T	-	971	0.878	Validation	Haem_ATL_59
TBL1XR1	nonsynonymous SNV	NM_024665	c.A421T	p.I141L	3	1.77E+08	1.77E+08	T	A	94	0.128	Validation	Haem_ATL_59
HLA-B	splicing	NM_005514	c.619+1G>A	NA	6	31323943	31323943	C	T	355	0.831	Validation	Haem_ATL_59
HLA-B	stopgain	NM_005514	c.G470A	p.W157X	6	31324093	31324093	C	T	564	0.172	Validation	Haem_ATL_59
CARD11	nonsynonymous SNV	NM_032415	c.C1865A	p.S622Y	7	2963942	2963942	G	T	841	0.29	Validation	Haem_ATL_59
CARD11	nonsynonymous SNV	NM_032415	c.T1864C	p.S622P	7	2963943	2963943	A	G	837	0.293	Validation	Haem_ATL_59
CARD11	nonsynonymous SNV	NM_032415	c.G1404C	p.R468S	7	2974201	2974201	C	G	1030	0.35	Validation	Haem_ATL_59
NOTCH1	frameshift deletion	NM_017617	c.7541_7542del	p.P2514fs	9	1.39E+08	1.39E+08	AG	-	858	0.388	Validation	Haem_ATL_59
GATA3	frameshift insertion	NM_002051	c.1302dupC	p.H434fs	10	8115955	8115955	-	C	984	0.383	Validation	Haem_ATL_59
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	684	0.466	Validation	Haem_ATL_59
TP53	nonsynonymous SNV	NM_000546	c.T658C	p.Y220H	17	7578191	7578191	A	G	894	0.427	Validation	Haem_ATL_59
TBL1XR1	nonsynonymous SNV	NM_024665	c.G931C	p.A311P	3	1.77E+08	1.77E+08	C	G	320	0.378	Validation	Haem_ATL_60
GPR183	stopgain	NM_004951	c.C259T	p.R87X	13	99948141	99948141	G	A	509	0.475	Validation	Haem_ATL_60
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	355	0.039	Validation	Haem_ATL_60
CD58	nonsynonymous SNV	NM_001779	c.G628A	p.G210S	1	1.17E+08	1.17E+08	C	T	359	0.844	Validation	Haem_ATL_61
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	2156	0.652	Validation	Haem_ATL_61
TBL1XR1	nonsynonymous SNV	NM_024665	c.G1122T	p.K374N	3	1.77E+08	1.77E+08	C	A	1398	0.927	Validation	Haem_ATL_61
HLA-B	nonframeshift deletion	NM_005514	c.379_402del	p.127_134del	6	31324161	31324184	GAGGAGGCGCCCGTCCGGCCCCAC	-	876	0.187	Validation	Haem_ATL_61
FYN	nonsynonymous SNV	NM_002037	c.A1592G	p.Y531C	6	1.12E+08	1.12E+08	T	C	772	0.03	Validation	Haem_ATL_61
CCR7	stopgain	NM_001838	c.C1060T	p.Q354X	17	38711071	38711071	G	A	1260	0.457	Validation	Haem_ATL_61
ZNF638	stopgain	NM_014497	c.G1423T	p.E475X	2	71591088	71591088	G	T	589	0.149	Validation	Haem_ATL_62
CCR4	stopgain	NM_005508	c.C1006T	p.Q336X	3	32995920	32995920	C	T	728	0.179	Validation	Haem_ATL_62
STAT3	nonsynonymous SNV	NM_003150	c.A1919T	p.Y640F	17	40474482	40474482	T	A	605	0.17	Validation	Haem_ATL_62
CARD11	nonsynonymous SNV	NM_032415	c.T389G	p.F130C	7	2984141	2984141	A	C	562	0.214	Validation	Haem_ATL_63
HNRNPA2B1	splicing	NM_031243	c.7-2->C	NA	7	26237488	26237488	-	G	393	0.359	Validation	Haem_ATL_63
TP53	stopgain	NM_000546	c.C406T	p.Q136X	17	7578524	7578524	G	A	624	0.482	Validation	Haem_ATL_63
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	970	0.328	Validation	Haem_ATL_63
CD58	frameshift deletion	NM_001779	c.642_643del	p.H214fs	1	1.17E+08	1.17E+08	TG	-	725	0.178	Validation	Haem_ATL_65
IRF2BP2	nonsynonymous SNV	NM_182972	c.G581A	p.G194D	1	2.35E+08	2.35E+08	C	T	361	0.244	Validation	Haem_ATL_65
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1195	0.299	Validation	Haem_ATL_65
IRF4	nonsynonymous SNV	NM_002460	c.C208G	p.L70V	6	393360	393360	C	G	336	0.045	Validation	Haem_ATL_65
ATXN1	nonsynonymous SNV	NM_000332	c.T1823A	p.L608Q	6	16326719	16326719	A	T	864	0.259	Validation	Haem_ATL_65
CARD11	nonsynonymous SNV	NM_032415	c.G2203A	p.E735K	7	2962334	2962334	C	T	772	0.07	Validation	Haem_ATL_65
CARD11	nonsynonymous SNV	NM_032415	c.T1852G	p.S618A	7	2963955	2963955	A	C	671	0.323	Validation	Haem_ATL_65
CARD11	nonsynonymous SNV	NM_032415	c.A761C	p.K254T	7	2979486	2979486	T	G	951	0.066	Validation	Haem_ATL_65
B2M	frameshift deletion	NM_004048	c.136_137del	p.Y46fs	15	45007689	45007690	TA	-	911	0.239	Validation	Haem_ATL_65
CCR4	frameshift insertion	NM_005508	c.967dupA	p.C322fs	3	32995880	32995880	-	A	2160	0.406	Validation	Haem_ATL_66
IRF4	nonsynonymous SNV	NM_002460	c.G341A	p.S114N	6	394945	394945	G	A	1061	0.608	Validation	Haem_ATL_66
VAV1	nonsynonymous SNV	NM_005428	c.A1211G	p.K404R	19	6828857	6828857	A	G	1325	0.281	Validation	Haem_ATL_66
CBLB	nonsynonymous SNV	NM_170662	c.T1125G	p.I375M	3	1.05E+08	1.05E+08	A	C	959	0.355	Validation	Haem_ATL_67
GATA3	frameshift insertion	NM_002051	c.225_226insCGTA	p.Y75fs	10	8097843	8097843	-	CGTA	721	0.51	Validation	Haem_ATL_67
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1081	0.563	Validation	Haem_ATL_67
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	1047	0.444	Validation	Haem_ATL_67
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	1031	0.444	Validation	Haem_ATL_68
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1339C	p.S447R	3	1.77E+08	1.77E+08	T	G	914	0.397	Validation	Haem_ATL_68
CSNK1A1	nonsynonymous SNV	NM_001892	c.C592G	p.Q198E	5	1.49E+08	1.49E+08	G	C	825	0.69	Validation	Haem_ATL_68
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	743	0.452	Validation	Haem_ATL_68
STAT3	nonsynonymous SNV	NM_003150	c.G1981C	p.D661H	17	40474420	40474420	C	G	962	0.035	Validation	Haem_ATL_68
VAV1	nonsynonymous SNV	NM_005428	c.A524T	p.E175V	19	6822306	6822306	A	T	371	0.035	Validation	Haem_ATL_68
PLCG1	nonsynonymous SNV	NM_002660	c.A2248G	p.M750V	20	39795446	39795446	A	G	765	0.027	Validation	Haem_ATL_68
PLCG1	nonsynonymous SNV	NM_002660	c.A3047T	p.Q1016L	20	39801202	39801202	A	T	821	0.051	Validation	Haem_ATL_68
GATA3	stopgain	NM_002051	c.G30A	p.W10X	10	8097648	8097648	G	A	646	0.472	Validation	Haem_ATL_69
GATA3	splicing	NM_002051	c.778+1G>A	NA	10	8100805	8100805	G	A	1249	0.479	Validation	Haem_ATL_69
TP53	nonsynonymous SNV	NM_000546	c.T470G	p.V157G	17	7578460	7578460	A	C	1177	0.962	Validation	Haem_ATL_69
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	1638	0.4	Validation	Haem_ATL_70
PRKCB	nonsynonymous SNV	NM_002738	c.G1597A	p.E533K	16	24196495	24196495	G	A	925	0.316	Validation	Haem_ATL_70
CSNK2A1	stopgain	NM_001895	c.G647A	p.W216X	20	470500	470500	C	T	996	0.238	Validation	Haem_ATL_70
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	1318	0.064	Validation	Haem_ATL_70
PLCG1	nonsynonymous SNV	NM_002660	c.T3499A	p.F1167I	20	39802396	39802396	T	A	1261	0.141	Validation	Haem_ATL_70
IRF2BP2	nonsynonymous SNV	NM_182972	c.G753C	p.Q251H	1	2.35E+08	2.35E+08	C	G	426	0.312	Validation	Haem_ATL_71
CBLB	splicing	NM_170662	c.2296+1G>-	NA	3	1.05E+08	1.05E+08	C	-	300	0.783	Validation	Haem_ATL_71
IRF4	nonsynonymous SNV	NM_002460	c.G358C	p.D120H	6	394962	394962	G	C	407	0.459	Validation	Haem_ATL_71
CSNK2B	stopgain	NM_001320	c.A529T	p.K177X	6	31637257	31637257	A	T	427	0.52	Validation	Haem_ATL_71
NOTCH1	stopgain	NM_017617	c.G7516T	p.E2506X	9	1.39E+08	1.39E+08	C	A	525	0.171	Validation	Haem_ATL_71
NOTCH1	frameshift deletion	NM_017617	c.7356_7362del	p.A2452fs	9	1.39E+08	1.39E+08	GTGCACC	-	402	0.187	Validation	Haem_ATL_71
IDH2	nonsynonymous SNV	NM_002168	c.G515A	p.R172K	15	90631838	90631838	C	T	439	0.253	Validation	Haem_ATL_71
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	430	0.486	Validation	Haem_ATL_71
CCR4	stopgain	NM_005508	c.C988T	p.Q330X	3	32995902	32995902	C	T	1709	0.784	Validation	Haem_ATL_72
TBL1XR1	nonsynonymous SNV	NM_024665	c.T965G	p.F322C	3	1.77E+08	1.77E+08	A	C	1136	0.378	Validation	Haem_ATL_72
TBL1XR1	stopgain	NM_024665	c.C313T	p.Q105X	3	1.77E+08	1.77E+08	G	A	1557	0.414	Validation	Haem_ATL_72
STAT3	nonsynonymous SNV	NM_003150	c.C1842A	p.S614R	17	40475068	40475068	G	T	1060	0.675	Validation	Haem_ATL_72
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	1249	0.054	Validation	Haem_ATL_72
PLCG1	nonsynonymous SNV	NM_002660	c.C1034T	p.S345F	20	39792584	39792584	C	T	1496	0.041	Validation	Haem_ATL_72
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	1579	0.415	Validation	Haem_ATL_72
CCR4	frameshift insertion	NM_005508	c.974dupT	p.L325fs	3	32995887	32995887	-	T	2283	0.272	Validation	Haem_ATL_73
TBL1XR1	nonsynonymous SNV	NM_024665	c.A920G	p.H307R	3	1.77E+08	1.77E+08	T	C	854	0.311	Validation	Haem_ATL_73
TBL1XR1	nonsynonymous SNV	NM_024665	c.A847C	p.S283R	3	1.77E+08	1.77E+08	T	G	1118	0.606	Validation	Haem_ATL_73
CSNK1A1	nonsynonymous SNV	NM_001892	c.G480T	p.L160F	5	1.49E+08	1.49E+08	C	A	977	0.16	Validation	Haem_ATL_73
IRF4	nonsynonymous SNV	NM_002460	c.C284A	p.T95K	6	394888	394888	C	A	1106	0.158	Validation	Haem_ATL_73
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	955	0.272	Validation	Haem_ATL_73
FAS	frameshift deletion	NM_000043	c.992delT	p.I331fs	10	90774191	90774191	T	-	1013	0.44	Validation	Haem_ATL_73
GPR183	frameshift insertion	NM_004951	c.501_502insTCCTC	p.I168fs	13	99947898	99947898	-	GAGGA	1446	0.355	Validation	Haem_ATL_73
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	969	0.448	Validation	Haem_ATL_73
PLCG1	nonsynonymous SNV	NM_002660	c.G3493C	p.D1165H	20	39802390	39802390	G	C	1319	0.157	Validation	Haem_ATL_73
TBL1XR1	nonsynonymous SNV	NM_024665	c.A920G	p.H307R	3	1.77E+08	1.77E+08	T	C	101	0.158	Validation	Haem_ATL_74
NOTCH1	frameshift insertion	NM_017617	c.7344_7345insCC	p.S2449fs	9	1.39E+08	1.39E+08	-	GG	147	0.041	Validation	Haem_ATL_74
NOTCH1	stopgain	NM_017617	c.C7246T	p.Q2416X	9	1.39E+08	1.39E+08	G	A	131	0.069	Validation	Haem_ATL_74
STAT3	nonsynonymous SNV	NM_003150	c.G1846A	p.E616K	17	40475064	40475064	C	T	165	0.139	Validation	Haem_ATL_74
CCR4	frameshift insertion	NM_005508	c.1001dupT	p.L334fs	3	32995914	32995914	-	T	773	0.415	Validation	Haem_ATL_75
TBL1XR1	nonsynonymous SNV	NM_024665	c.T1059A	p.N353K	3	1.77E+08	1.77E+08	A	T	294	0.483	Validation	Haem_ATL_75
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	390	0.344	Validation	Haem_ATL_75
TP53	nonsynonymous SNV	NM_000546	c.G856A	p.E286K	17	7577082	7577082	C	T	479	0.309	Validation	Haem_ATL_75
TP53	nonsynonymous SNV	NM_000546	c.C817T	p.R273C	17	7577121	7577121	G	A	421	0.33	Validation	Haem_ATL_75
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	491	0.295	Validation	Haem_ATL_75
PLCG1	nonframeshift deletion	NM_002660	c.3487_3489del	p.1163_1163del	20	39802384	39802386	GAG	-	604	0.265	Validation	Haem_ATL_75
HLA-B	stopgain	NM_005514	c.C796T	p.Q266X	6	31323193	31323193	G	A	703	0.119	Validation	Haem_ATL_76
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	685	0.028	Validation	Haem_ATL_76
VAV1	nonsynonymous SNV	NM_005428	c.G1666A	p.E556K	19	6833594	6833594	G	A	639	0.083	Validation	Haem_ATL_76
CD58	stopgain	NM_001779	c.C635G	p.S212X	1	1.17E+08	1.17E+08	G	C	863	0.076	Validation	Haem_ATL_77
CCR4	stopgain	NM_005508	c.C993A	p.Y331X	3	32995907	32995907	C	A	1698	0.227	Validation	Haem_ATL_77
RHOA	nonsynonymous SNV	NM_001664	c.G47A	p.C16Y	3	49412976	49412976	C	T	1457	0.085	Validation	Haem_ATL_77
TBL1XR1	nonsynonymous SNV	NM_024665	c.A1184G	p.Y395C	3	1.77E+08	1.77E+08	T	C	1069	0.299	Validation	Haem_ATL_77
TET2	nonframeshift deletion	NM_001127208	c.3580_3594del	p.1194_1198del	4	1.06E+08	1.06E+08	CCTATTGCTAAGTGG	-	1804	0.118	Validation	Haem_ATL_77
TET2	frameshift insertion	NM_001127208	c.3975dupT	p.H1325fs	4	1.06E+08	1.06E+08	-	T	1717	0.255	Validation	Haem_ATL_77
CARD11	nonsynonymous SNV	NM_032415	c.A2677T	p.S893C	7	2956950	2956950	T	A	1019	0.353	Validation	Haem_ATL_77
IRF2BP2	nonsynonymous SNV	NM_182972	c.C629T	p.A210V	1	2.35E+08	2.35E+08	G	A	349	0.037	Validation	Haem_ATL_78
IRF4	nonsynonymous SNV	NM_002460	c.A176G	p.K59R	6	393328	393328	A	G	681	0.069	Validation	Haem_ATL_78
PRKCB	nonsynonymous SNV	NM_002738	c.G1408C	p.D470H	16	24192124	24192124	G	C	1147	0.083	Validation	Haem_ATL_78
PLCG1	nonsynonymous SNV	NM_002660	c.C142T	p.R48W	20	39766423	39766423	C	T	1063	0.044	Validation	Haem_ATL_78
IRF4	nonsynonymous SNV	NM_002460	c.T347G	p.L116R	6	394951	394951	T	G	1023	0.33	Validation	Haem_ATL_79
HLA-B	stopgain	NM_005514	c.G470A	p.W157X	6	31324093	31324093	C	T	1254	0.226	Validation	Haem_ATL_79
CARD11	nonsynonymous SNV	NM_032415	c.G1876A	p.E626K	7	2963931	2963931	C	T	1325	0.053	Validation	Haem_ATL_79
CARD11	nonsynonymous SNV	NM_032415	c.C1071A	p.D357E	7	2977613	2977613	G	T	1597	0.495	Validation	Haem_ATL_79
HNRNPA2B1	splicing	NM_002137	c.842-1G>A	NA	7	26232994	26232994	C	T	1303	0.55	Validation	Haem_ATL_79
NOTCH1	stopgain	NM_017617	c.C7501T	p.Q2501X	9	1.39E+08	1.39E+08	G	A	911	0.098	Validation	Haem_ATL_79
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1041	0.061	Validation	Haem_ATL_79

Supplemental Table 2. Somatic mutations detected by targeted capture sequencing in 183 ATL cases

Gene	Type of mutation	Accession number	Base change	Amino acid change	Chromosome	Start	End	Ref	Alt	Depth	Variant allele frequency	Cohort	Case ID
PRKCB	nonsynonymous SNV	NM_002738	c.G1597A	p.E533K	16	24196495	24196495	G	A	999	0.292	Validation	Haem_ATL_79
CCR7	stopgain	NM_001838	c.C1060T	p.Q354X	17	38711071	38711071	G	A	1343	0.312	Validation	Haem_ATL_79
CCR7	stopgain	NM_001838	c.C1051T	p.Q351X	17	38711080	38711080	G	A	1370	0.074	Validation	Haem_ATL_79
PLCG1	nonframeshift deletion	NM_002660	c.3482_3496del	p.1161_1166del	20	39802379	39802393	TGTATGAGGAAGACA	-	1531	0.197	Validation	Haem_ATL_79
CCR4	stopgain	NM_005508	c.C988T	p.Q330X	3	32995902	32995902	C	T	1139	0.216	Validation	Haem_ATL_80
CDKN2A	stopgain	NM_000077	c.C238T	p.R80X	9	21971120	21971120	G	A	590	0.044	Validation	Haem_ATL_80
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	801	0.248	Validation	Haem_ATL_80
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	1163	0.411	Validation	Haem_ATL_80
CCR4	frameshift insertion	NM_005508	c.968dupG	p.R323fs	3	32995881	32995881	-	G	1807	0.356	Validation	Haem_ATL_81
CSNK1A1	nonsynonymous SNV	NM_001892	c.G86A	p.G29E	5	1.49E+08	1.49E+08	C	T	1141	0.387	Validation	Haem_ATL_81
CSNK2B	nonframeshift deletion	NM_001320	c.569_571del	p.190_191del	6	31637624	31637626	TCA	-	1210	0.36	Validation	Haem_ATL_81
POT1	stopgain	NM_015450	c.G226T	p.G76X	7	1.25E+08	1.25E+08	C	A	1656	0.571	Validation	Haem_ATL_81
FAS	frameshift deletion	NM_000043	c.63_66del	p.K21fs	10	90762818	90762821	AAGT	-	3369	0.254	Validation	Haem_ATL_81
FAS	nonsynonymous SNV	NM_000043	c.G67T	p.V23F	10	90762822	90762822	G	T	2727	0.276	Validation	Haem_ATL_81
FAS	splicing	NM_000043	c.677-2A>T	NA	10	90773874	90773874	A	T	1187	0.129	Validation	Haem_ATL_81
PRKCB	nonsynonymous SNV	NM_002738	c.G1279A	p.D427N	16	24183630	24183630	G	A	1370	0.55	Validation	Haem_ATL_81
PLCG1	nonframeshift deletion	NM_002660	c.3482_3496del	p.1161_1166del	20	39802379	39802393	TGTATGAGGAAGACA	-	1699	0.249	Validation	Haem_ATL_81
PLCG1	nonsynonymous SNV	NM_002660	c.T3501G	p.F1167L	20	39802398	39802398	T	G	1294	0.321	Validation	Haem_ATL_81
CCR4	stopgain	NM_005508	c.C993G	p.Y331X	3	32995907	32995907	C	G	1488	0.304	Validation	Haem_ATL_82
STAT3	nonsynonymous SNV	NM_003150	c.G1981T	p.D661Y	17	40474420	40474420	C	A	1150	0.404	Validation	Haem_ATL_82
VAV1	nonsynonymous SNV	NM_005428	c.A1211G	p.K404R	19	6828857	6828857	A	G	1088	0.851	Validation	Haem_ATL_82
PLCG1	nonsynonymous SNV	NM_002660	c.C2617T	p.R873W	20	39798133	39798133	C	T	664	0.474	Validation	Haem_ATL_82
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	1103	0.423	Validation	Haem_ATL_82
HNRNPA2B1	stopgain	NM_002137	c.G964T	p.G322X	7	26232871	26232871	C	A	921	0.244	Validation	Haem_ATL_83
PLCG1	nonsynonymous SNV	NM_002660	c.G3487A	p.E1163K	20	39802384	39802384	G	A	1109	0.256	Validation	Haem_ATL_83
CCR4	frameshift deletion	NM_005508	c.538_547del	p.T180fs	3	32995452	32995461	ACTGAGCGCA	-	914	0.316	Validation	Haem_ATL_84
PRKCB	nonsynonymous SNV	NM_002738	c.A1637T	p.E546V	16	24196803	24196803	A	T	616	0.494	Validation	Haem_ATL_84

Supplemental Table 3. Clinical variables and risk factors associated with gene mutations ($p < 0.05$ in uncorrected analyses).

Clinical variable/ risk factor	Gene	Mutation frequency [vs no risk factor]	p	Corrected p*
Sex (male gender)	*NA*			
Subtype (acute or unfavorable chronic)	*NA*			
Stage 3–4	*NA*			
ECOG PS 2–4	*TET2*	4 (23.5) [4 (4.9)]	0.038	0.684
Alb < 3.5 g/dL	*VAV1*	15 (33.3) [5 (9.3)]	0.007	0.126
	IRF4	15 (33.3) [7 (13.0)]	0.029	0.522
cCa ≥ 11 mg/dL	*PRKCB*	10 (62.5) [19 (22.9)]	0.004	0.072
	VAV1	8 (50.0) [12 (14.5)]	0.004	0.072
sIL-2R ≥ 20000 U/mL	*TBL1XR1*	5 (11.1) [16 (29.6)]	0.046	0.828
CRP ≥ 2.5 mg/dL	*VAV1*	8 (40.0) [12 (15.2)]	0.031	0.558
ATL-PI high- or intermediate-risk	*VAV1*	19 (31.1) [1 (2.6)]	0.001	0.018

*Correction for multiple testing by Bonferroni–Holm. NA, not applicable, indicates that no genes were associated with that clinical variable/risk factor at $p < 0.05$ in uncorrected analyses; ECOG, Eastern Cooperative Oncology Group; PS, Performance Status; ATL-PI, Adult T-cell leukemia/lymphoma prognostic index.

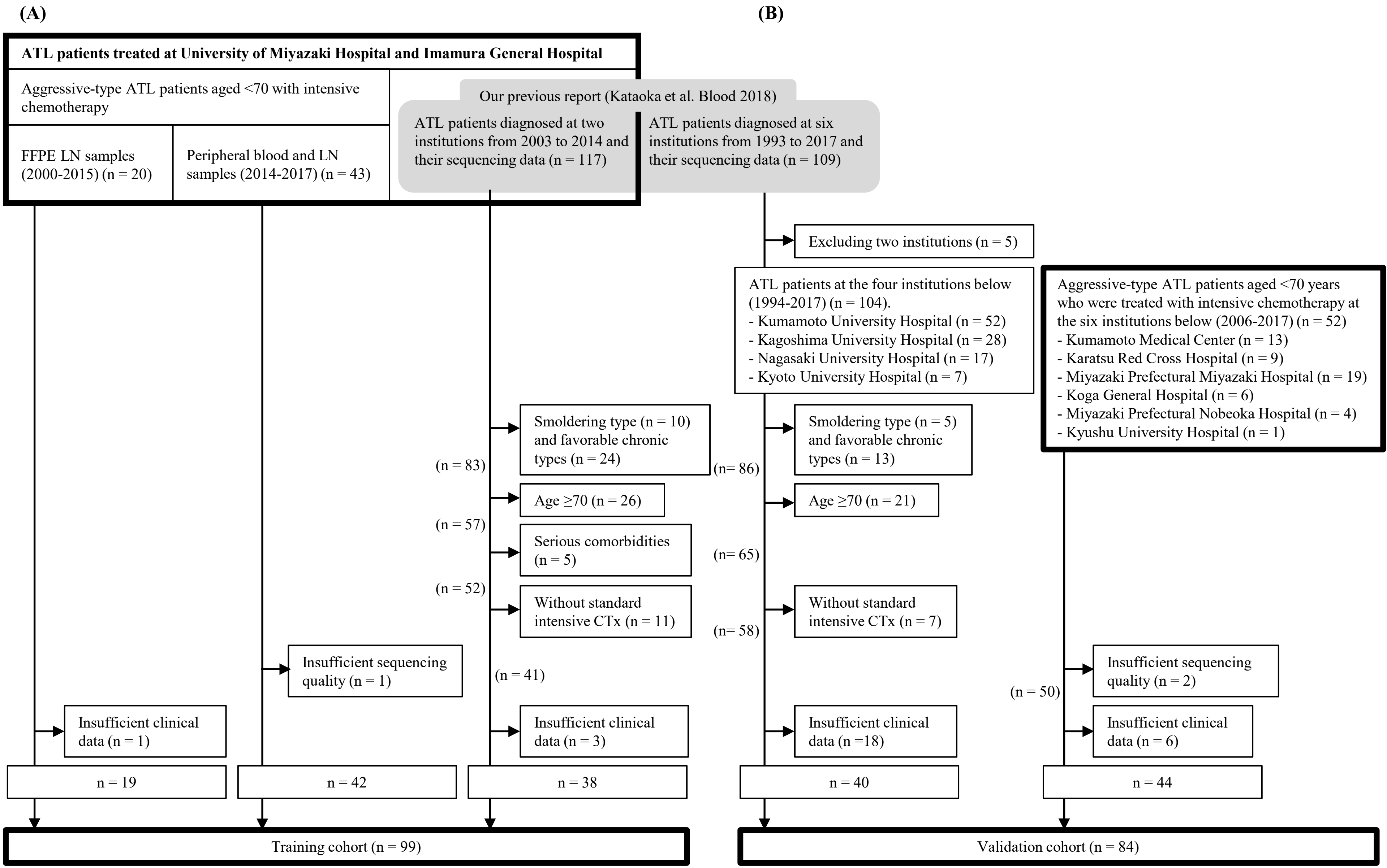
Supplemental Table 4. Elastic-net coefficients of ATL-PI risk categories and mutation status in 13 genes.

Variable	Elastic-net coefficient
Clinical risk factors	
ATL-PI high-risk	1.053
ATL-PI intermediate-risk	0
ATL-PI low-risk	-0.363
Genetic risk factors	
TP53 mutation	0.413
IRF4 mutation	0.263
RHOA mutation	0.109
PRKCB mutation	0.079
CARD11 mutation	0.056
CCR4 mutation	0
NOTCH1 mutation	0
PLCG1 mutation	0
STAT3 mutation	0
TBL1XR1 mutation	0
VAV1 mutation	0
CCR7 mutation	-0.195
GATA3 mutation	-0.252

For the elastic-net penalized Cox regression, binarized ATL-PI risk categories and mutation status in 13 genes were used as variables. The elastic-net penalized Cox regression shrank coefficients and set those of one clinical and six genetic variables to zero, under the optimal parameters (alpha = 0.22, lambda = 0.176). The m7-ATLPI was then developed by integrating the remaining two clinical variables (ATL-PI high-risk and ATL-PI low-risk) and seven genetic variables (mutations in *TP53*, *IRF4*, *RHOA*, *PRKCB*, *CARD11*, *CCR7*, and *GATA3*). Variables were ordered by their coefficients. Abbreviations: ATL-PI, Adult T-cell leukemia/lymphoma prognostic index.

Supplemental Figures

Supplemental Figure 1

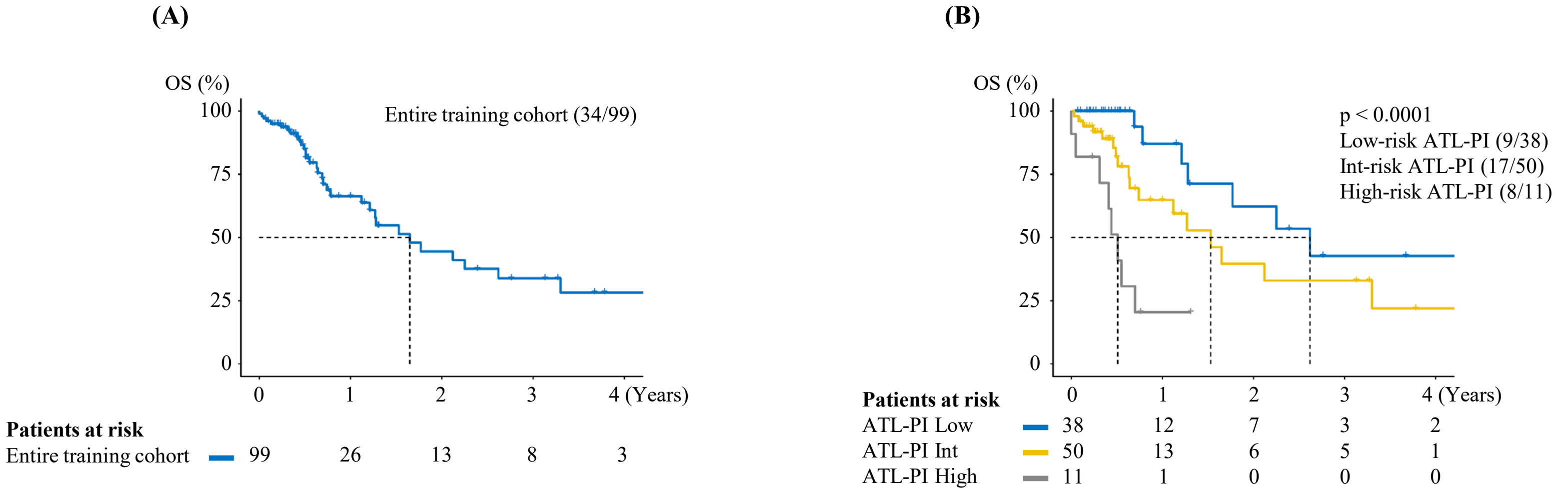


Supplemental Figure 1. Patient flow in this study.

(A) Training cohort. Peripheral blood and LN samples (n = 43) and FFPE LN samples (n = 20) were obtained from aggressive-type ATL patients who were <70 years old and who received intensive chemotherapy and were analyzed by targeted sequencing in this study. The analysis also included 41 samples and their sequencing data from aggressive-type ATL patients in our previous study who were <70 years old and who received intensive chemotherapy; their clinical information, including outcomes, was updated[3]. Excluding samples with insufficient clinical data or sequencing quality, 99 samples were included in the training cohort. FFPE, formalin-fixed paraffin-embedded; LN, lymph node; CTx, chemotherapy.

(B) Validation cohort. Fifty-two samples were obtained from aggressive-type ATL patients who were <70 years old and who received intensive chemotherapy and were analyzed by targeted sequencing in this study. The analysis also included 58 samples and their sequencing data from aggressive-type ATL patients in our previous study who were <70 years old and who received intensive chemotherapy; their clinical information, including outcomes, was updated[3]. Excluding samples with insufficient clinical data or sequencing quality, 84 samples were included in the validation cohort.

Supplemental Figure 2



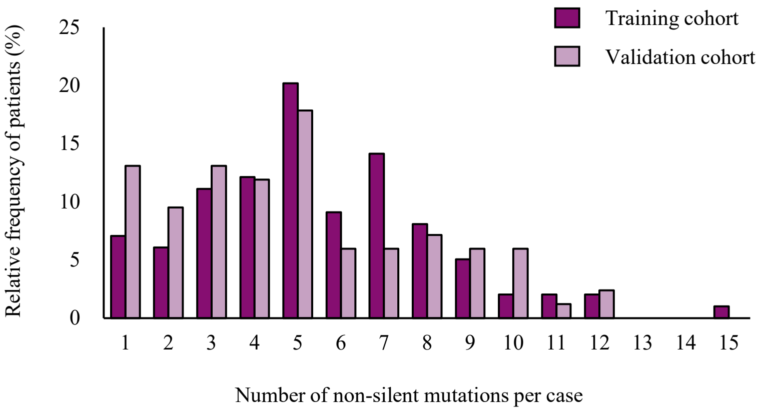
Supplemental Figure 2. Overall survival of the training cohort.

(A) Kaplan-Meier OS curves of the entire training cohort.

(B) Kaplan-Meier OS curves of the training cohort stratified by ATL-PI category.

Numbers in parentheses show number of patients with events / number of patients per cohort.

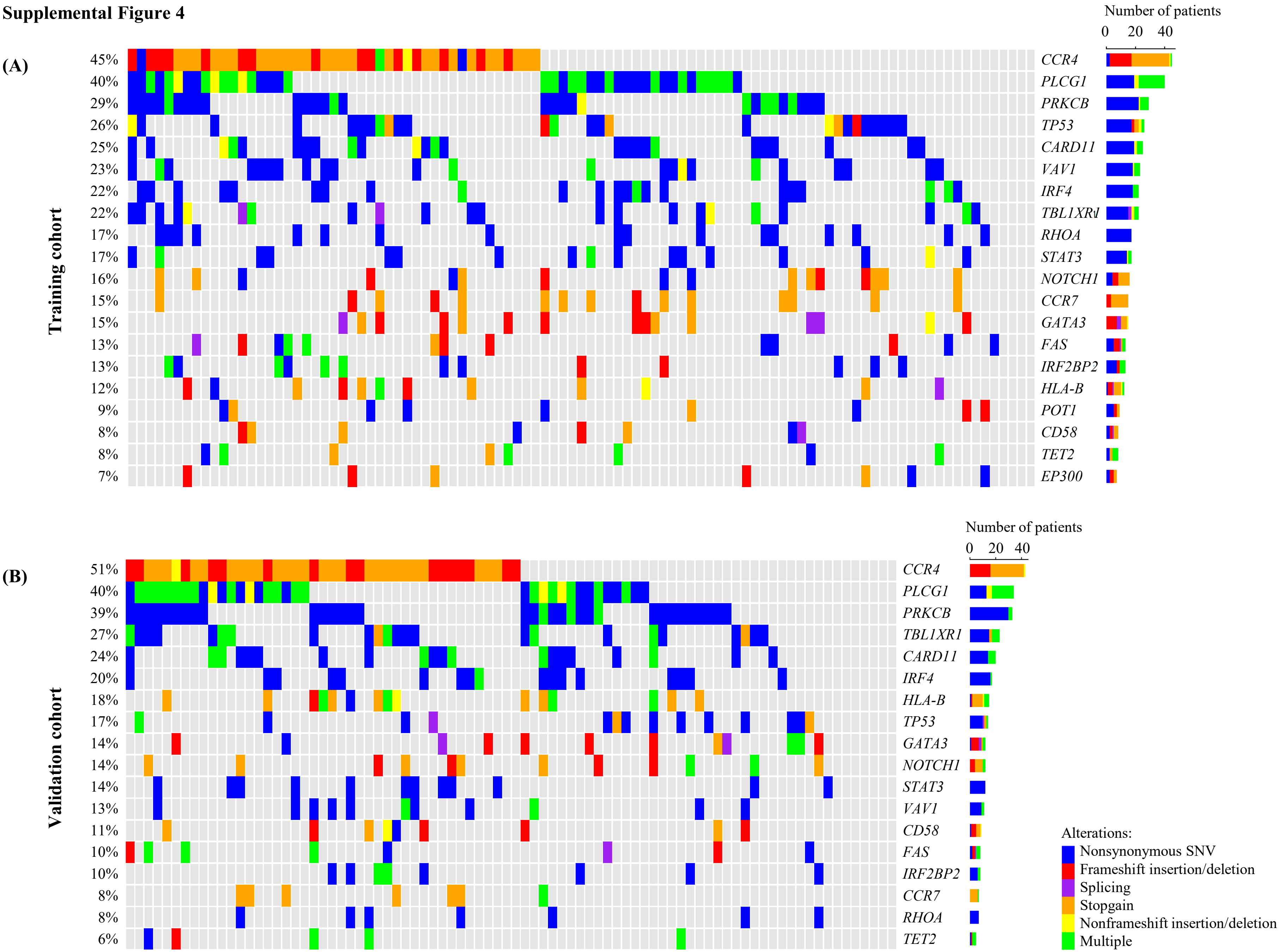
Supplemental Figure 3



Supplementary Figure 3. Distribution of cases in the training and validation cohorts by the number of genes with non-silent mutations.

The median number of mutated genes determined by targeted sequencing in each patient was five (IQR 4–7) in the training cohort and five (IQR 3–7) in the validation cohort.

Supplemental Figure 4



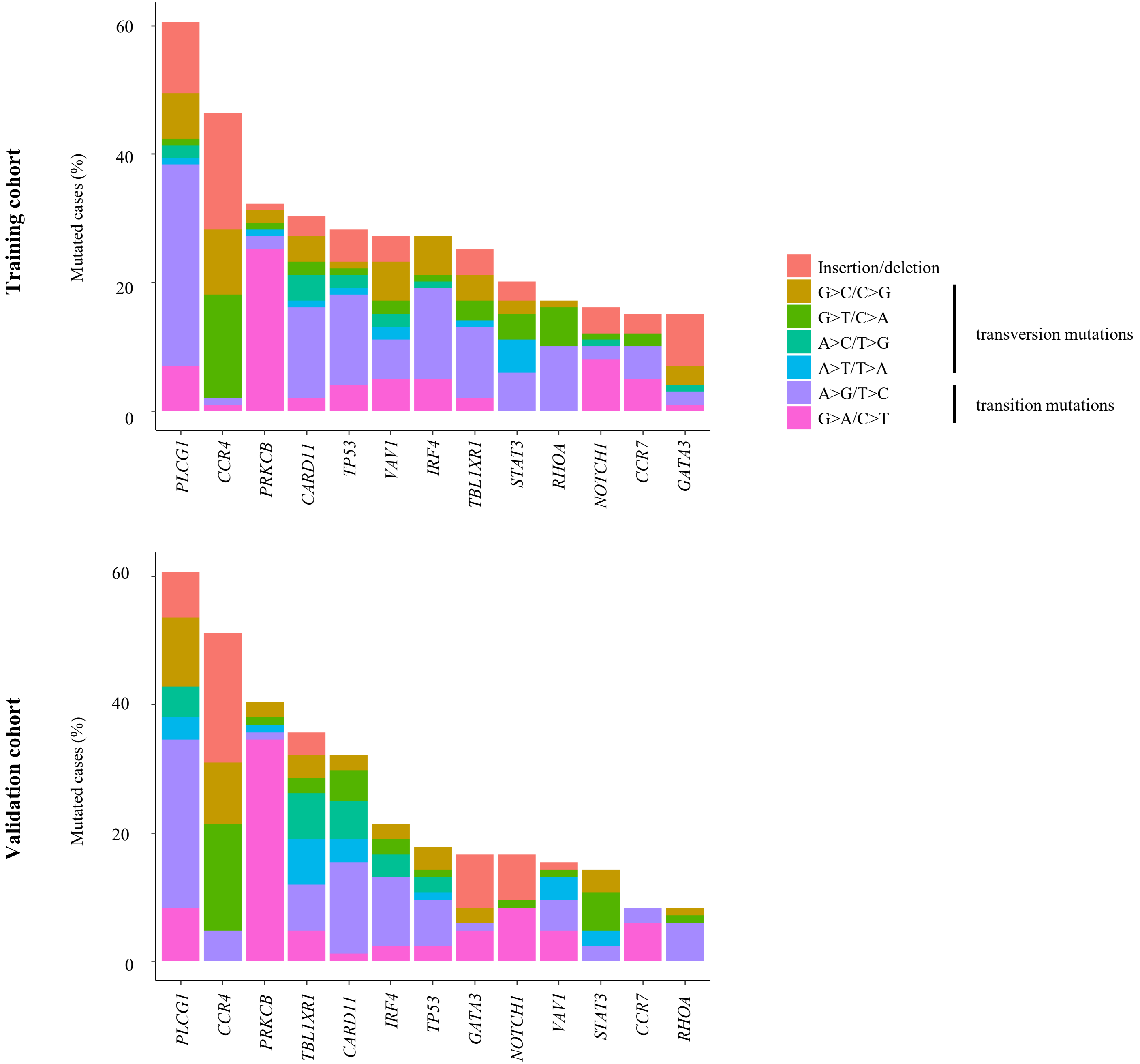
Supplemental Figure 4. The targeted mutational landscape in the training and validation cohorts.

(A) Mutation plot for 99 patients in the training cohort. Twenty mutated genes with non-silent mutations in >5% of cases are shown.

(B) Mutation plot for 84 patients in the validation cohort. Eighteen mutated genes with non-silent mutations in >5% of cases are shown.

Mutation types are color coded. For all genes, non-silent variants with variant allele frequencies >0.1 are shown. Genes are ordered by frequency. The predicted functional impact of missense mutations was determined by the Mutation Assessor tool. Mutation types are indicated in the graph legend.

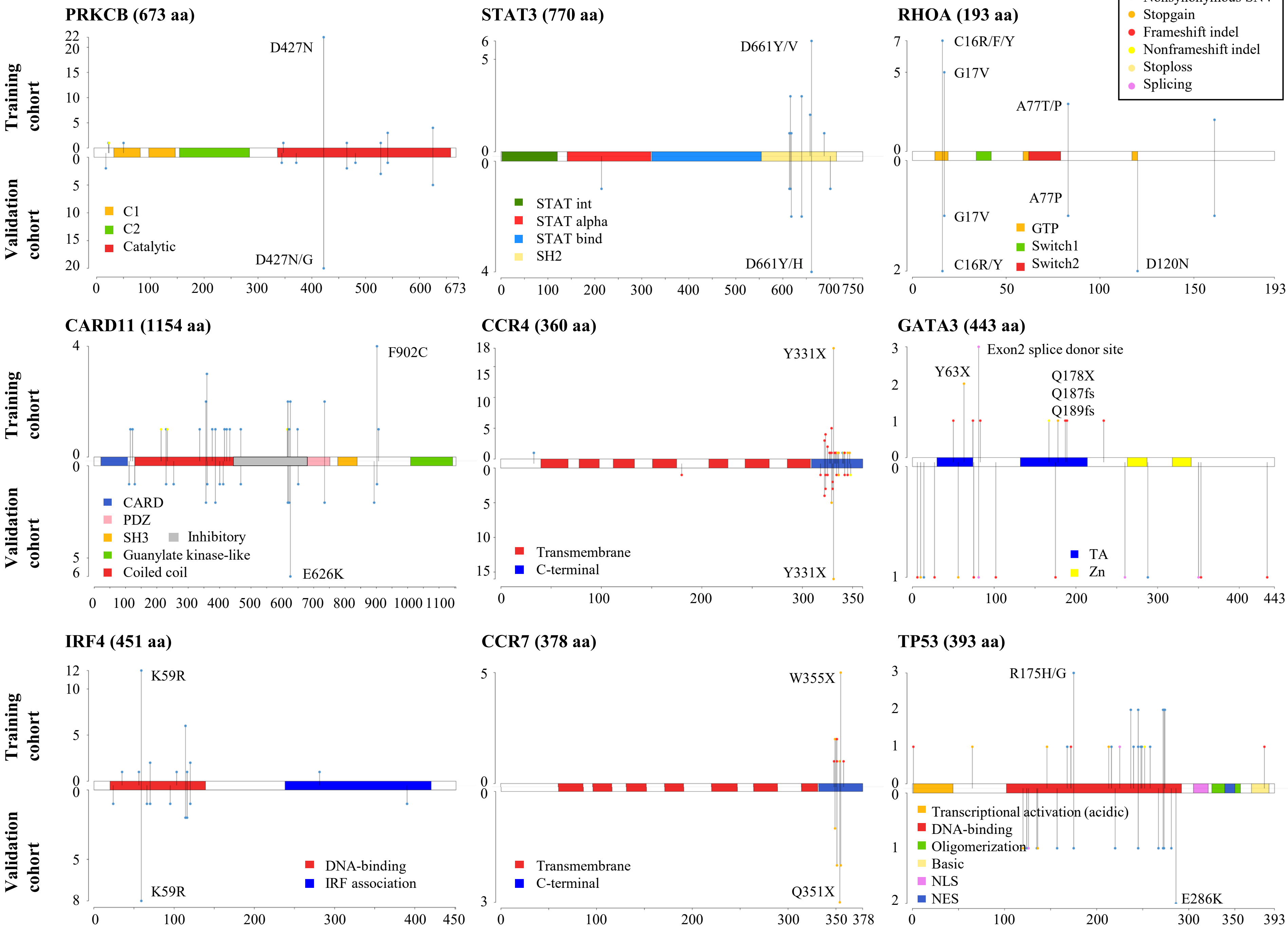
Supplemental Figure 5



Supplemental Figure 5. Frequencies of transitions, transversions, and small insertions/deletions in the training and validation cohorts.

Types of alterations are indicated in the graph legend.

Supplemental Figure 6

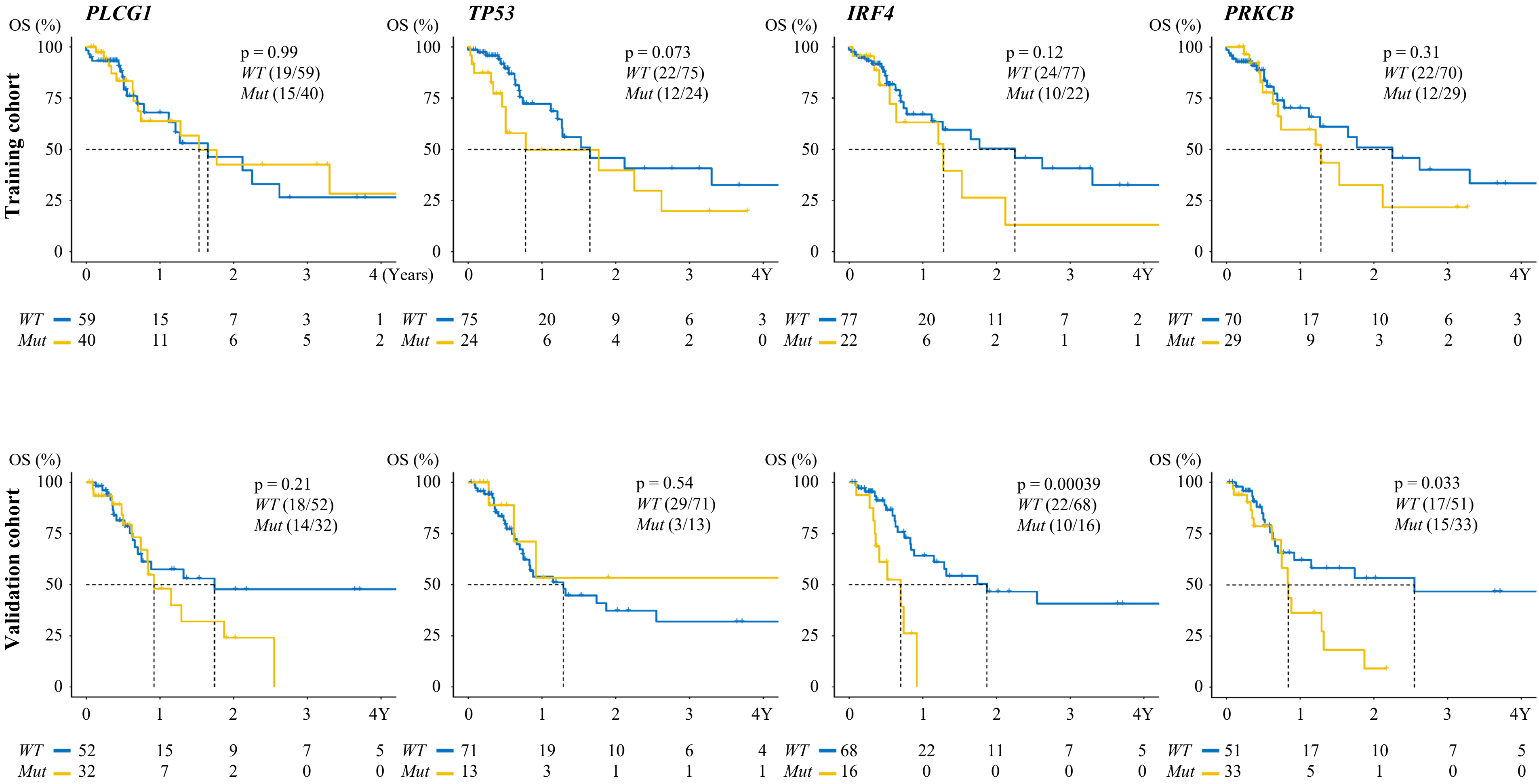


Supplemental Figure 6. Selected genes with hotspot mutations.

Mutations in the training cohort are shown on top, and those in the validation cohort are shown below. Truncating mutations consist of nonsense, nonstop, frameshift deletion, frameshift insertion, and splice site mutations. In the training cohort, mutations in *PRKCB* were clustered at the catalytic domain (32 [91%] of 35). Many *CARD11* mutations were clustered in the coiled-coil domain (14 [45%] of 31) and inhibitory domain (8 [26%] of 31). Almost all *IRF4* mutations (26 [96%] of 27) were clustered in the DNA-binding domain, and all were missense mutations. All *STAT3* mutations (17 [100%] of 17) were clustered in the SH2 domain. Almost all *CCR4* and *CCR7* mutations (45 [98%] of 46; and 15 [100%] of 15) occurred in the cytoplasmic regions. Many *RHOA* mutations (12 [71%] of 17) were clustered in the guanosine triphosphate (GTP)-binding domain, as previously reported[6]. Many *GATA3* mutations (12 [92%] of 13) were clustered in the transactivation domain and were mostly frameshift or splicing mutations. Many *TP53* mutations were clustered in the DNA-binding domain (25 [89%] of 28). In the validation cohort, the mutations were similarly distributed.

Supplemental Figure 7

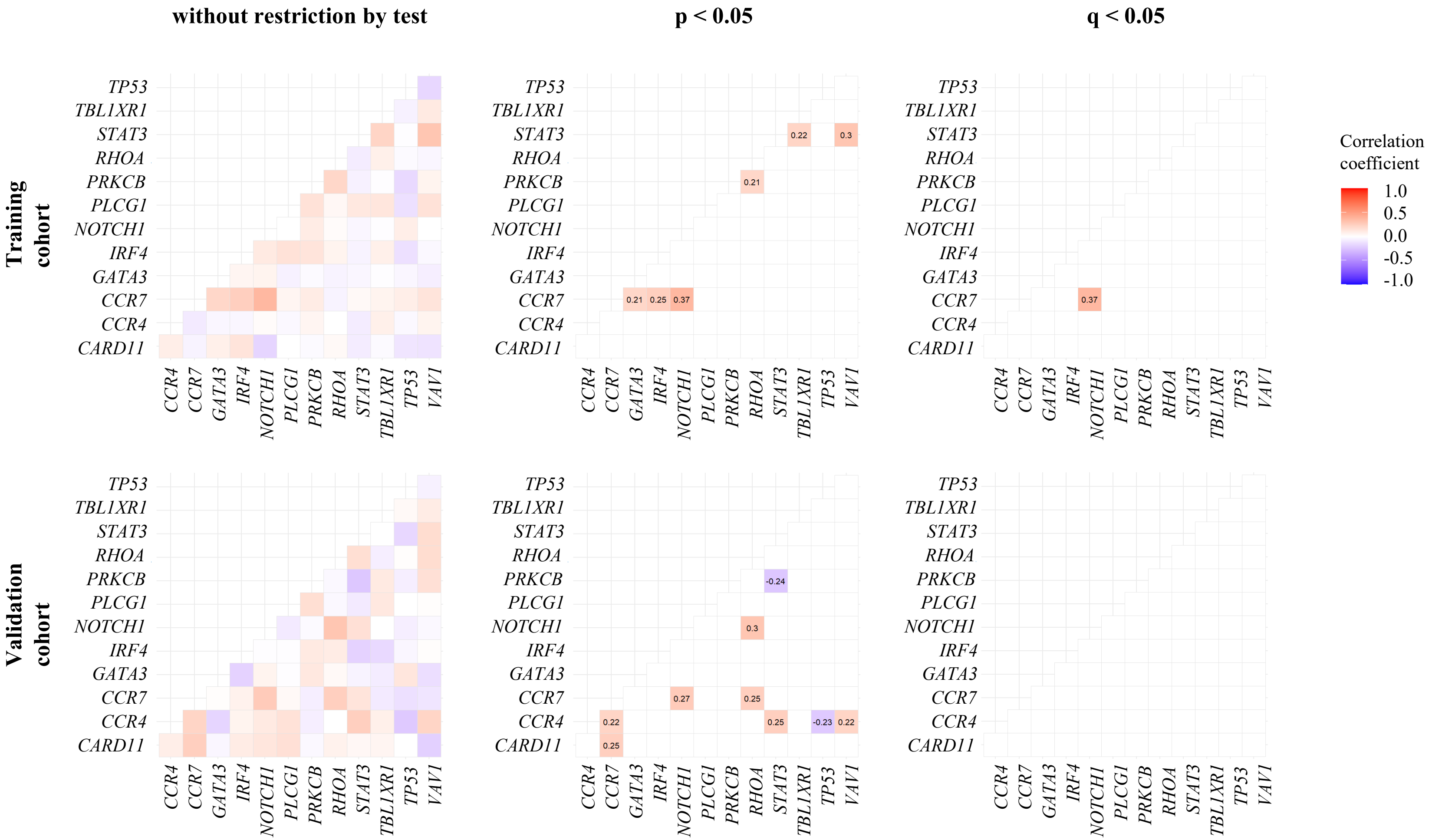
	Univariate					Univariate adjusted for ATL-PI				
Cohort	**Gene**	**β**	**HR**	**p**	**Corrected p**	**Gene**	**β**	**HR**	**p**	**Corrected p**
Training cohort	*TP53*	0.65	1.92	0.077	1.000	*TP53*	0.75	2.11	0.044	0.843
Validation cohort	*IRF4*	1.39	4.01	0.001	0.019	*IRF4*	1.30	3.65	0.002	0.092
	PRKCB	0.78	2.17	0.037	0.666	*PRKCB*	0.66	1.94	0.078	1.000



Supplemental Figure 7. Kaplan-Meier curves for genetic variants that significantly affected OS in either cohort by univariate analysis with or without adjustment.

A summary of unadjusted and adjusted univariable test results is shown. Multiple hypothesis correction was performed by the Bonferroni-Holm procedure. HR, hazard ratio; ATL-PI, adult T-cell leukemia/lymphoma prognostic index; *WT*, *wild type*; *Mut*, *mutated*. Numbers on Kaplan-Meier OS curves indicate number of patients with event / number of patients per cohort.

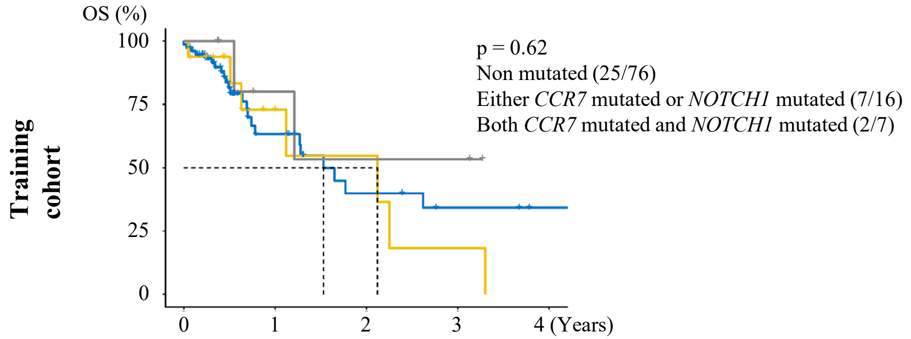
Supplemental Figure 8



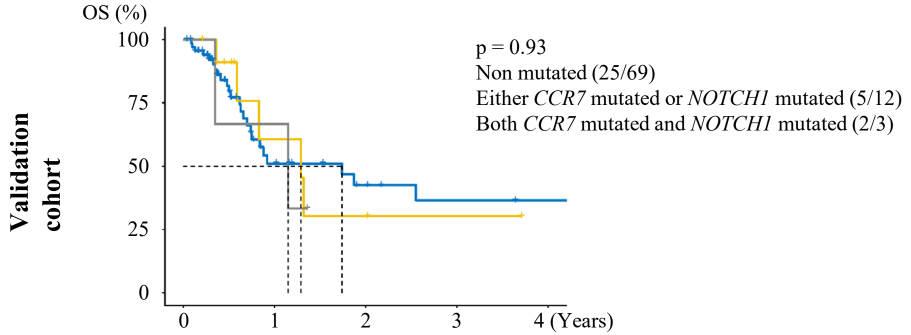
Supplemental Figure 8. Correlation matrix analysis.

A heatmap is shown of all Pearson's correlation coefficients for pairwise combinations of the 13 most commonly mutated genes in the training and validation cohorts. Pearson's r correlation coefficients without restriction (left), with $p < 0.05$ (middle), and with $q < 0.05$ (right) are shown.

Supplemental Figure 9



Patients at risk		0	1	2	3	4
Non mutated	🟦	76	18	8	5	3
Either *CCR7* mutated or *NOTCH1* mutated	🟨	16	5	3	1	0
Both *CCR7* mutated and *NOTCH1* mutated	⬜	7	3	2	2	0

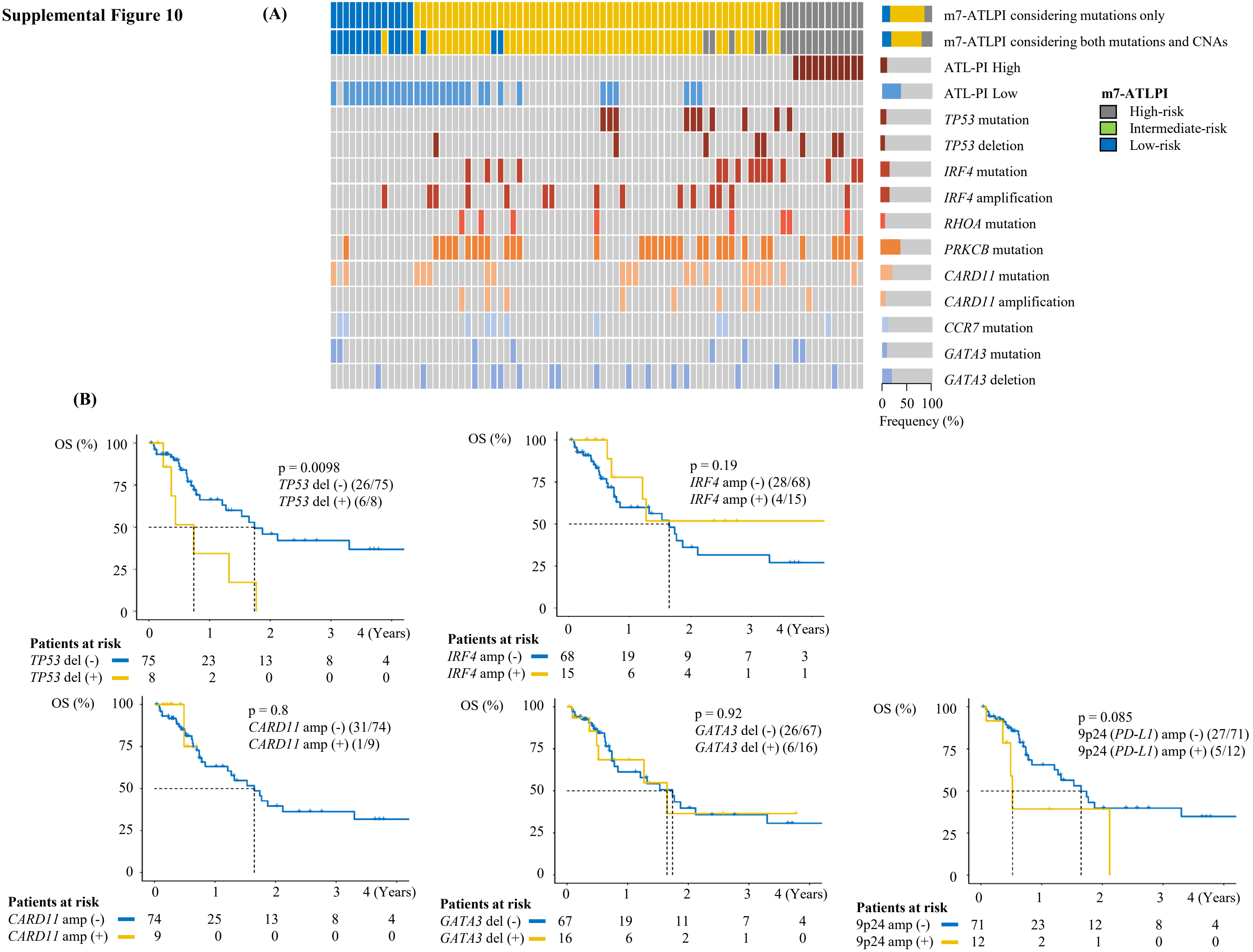


Patients at risk		0	1	2	3	4
Non mutated	🟦	69	16	9	6	5
Either *CCR7* mutated or *NOTCH1* mutated	🟨	12	4	2	1	0
Both *CCR7* mutated and *NOTCH1* mutated	⬜	3	2	0	0	0

Supplemental Figure 9. Kaplan-Meier curves classified by the status of mutational combinations in both cohorts.

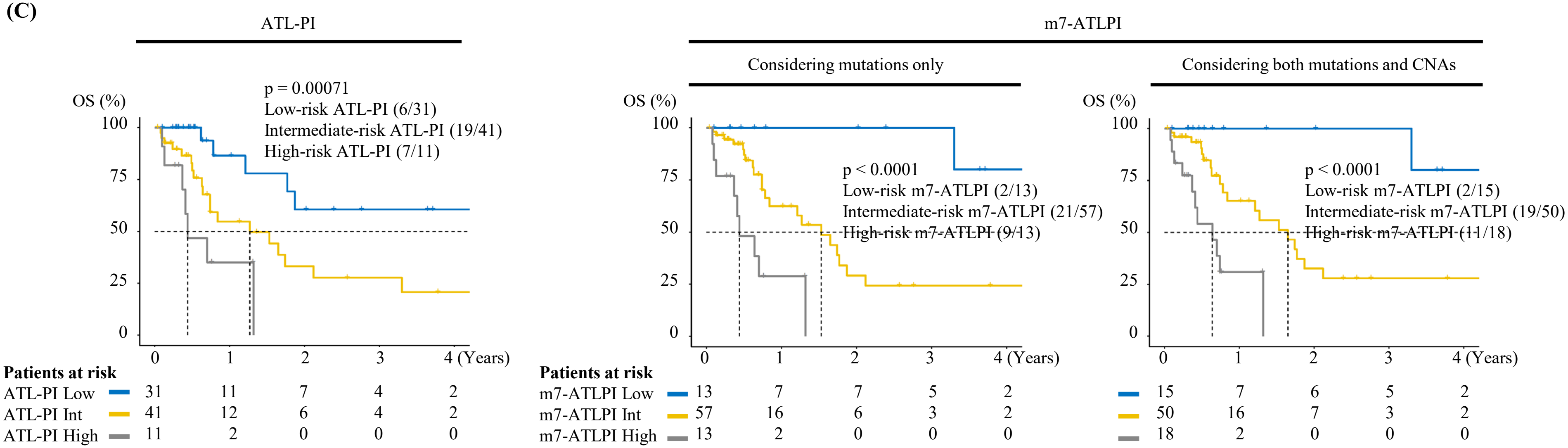
Survival curves classified by the status of the mutational combinations of *NOTCH1* and *CCR7* are shown. Numbers on Kaplan-Meier OS curves indicate number of patients with events / number of patients per cohort.

Supplemental Figure 10



Supplemental Figure 10 (Continued)

(C)



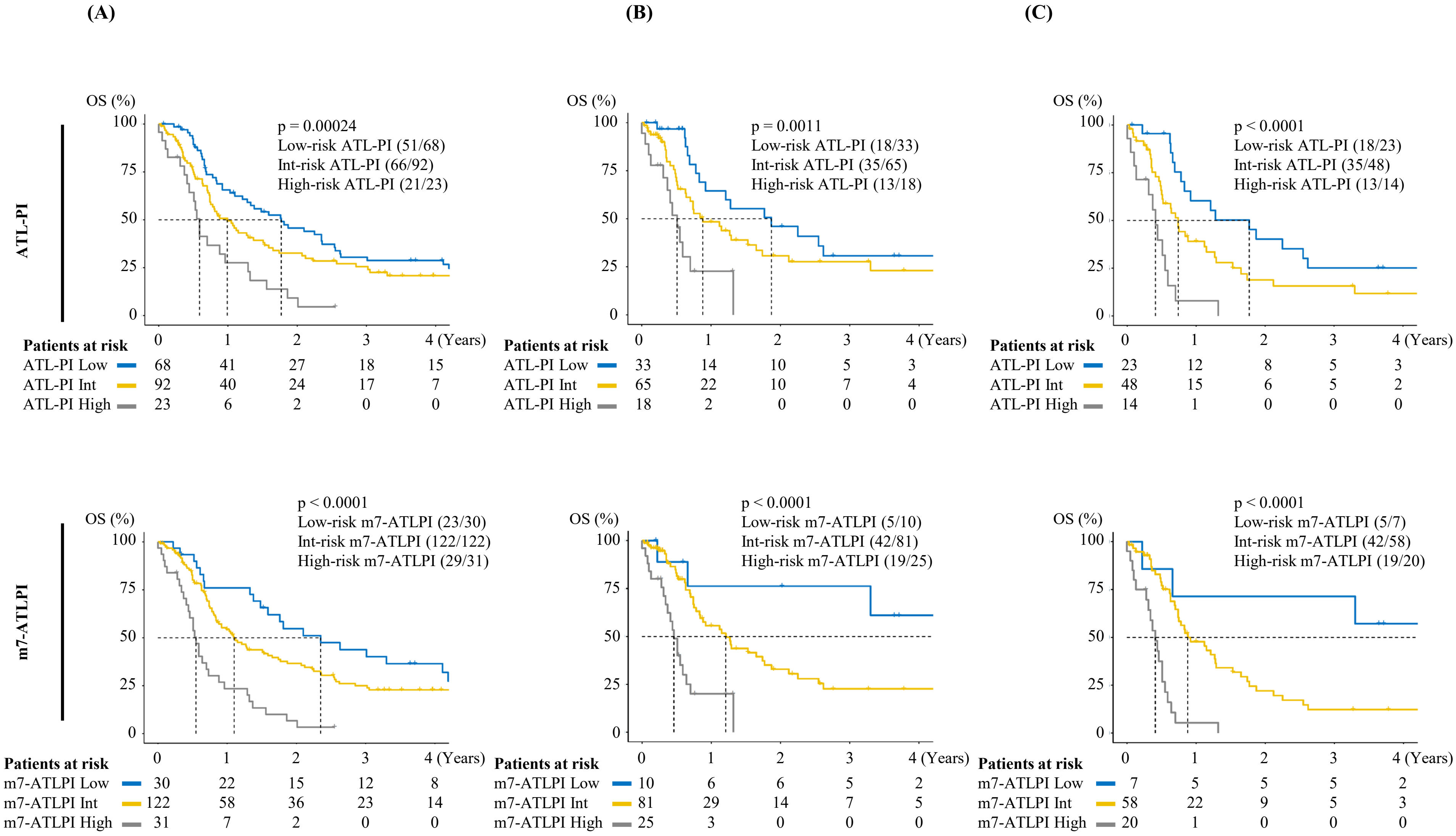
Supplemental Figure 10. m7-ATLPI considering both mutations and CNAs as risk factors.

(A) Comparison of risk categories defined by the m7-ATLPI considering mutations only vs. both mutations and CNAs. m7-ATLPI categorizations of patients according to mutations and/or CNA data are shown along with clinical (ATL-PI categories) and molecular predictors. Boxes indicate high- or low-risk ATL-PI categories, or mutations or CNAs in the indicated genes. Color codes indicate coefficients of individual m7-ATLPI predictors.

(B) Kaplan-Meier curves classified by the presence or absence of CNAs for four genes (*TP53*, *IRF4*, *CARD11*, and *GATA3*) and 9p24 (*PD-L1*). Del, deletion; amp, amplification.

(C) OS of patients based on mutation and CNA data. OS is stratified by the ATL-PI, m7-ATLPI considering mutations only, and m7-ATLPI considering both mutations and CNAs.

Supplemental Figure 11



(A)

Patients at risk	0	1	2	3	4 (Years)
ATL-PI Low	68	41	27	18	15
ATL-PI Int	92	40	24	17	7
ATL-PI High	23	6	2	0	0

Patients at risk	0	1	2	3	4 (Years)
m7-ATLPI Low	30	22	15	12	8
m7-ATLPI Int	122	58	36	23	14
m7-ATLPI High	31	7	2	0	0

(B)

Patients at risk	0	1	2	3	4 (Years)
ATL-PI Low	33	14	10	5	3
ATL-PI Int	65	22	10	7	4
ATL-PI High	18	2	0	0	0

Patients at risk	0	1	2	3	4 (Years)
m7-ATLPI Low	10	6	6	5	2
m7-ATLPI Int	81	29	14	7	5
m7-ATLPI High	25	3	0	0	0

(C)

Patients at risk	0	1	2	3	4 (Years)
ATL-PI Low	23	12	8	5	3
ATL-PI Int	48	15	6	5	2
ATL-PI High	14	1	0	0	0

Patients at risk	0	1	2	3	4 (Years)
m7-ATLPI Low	7	5	5	5	2
m7-ATLPI Int	58	22	9	5	3
m7-ATLPI High	20	1	0	0	0

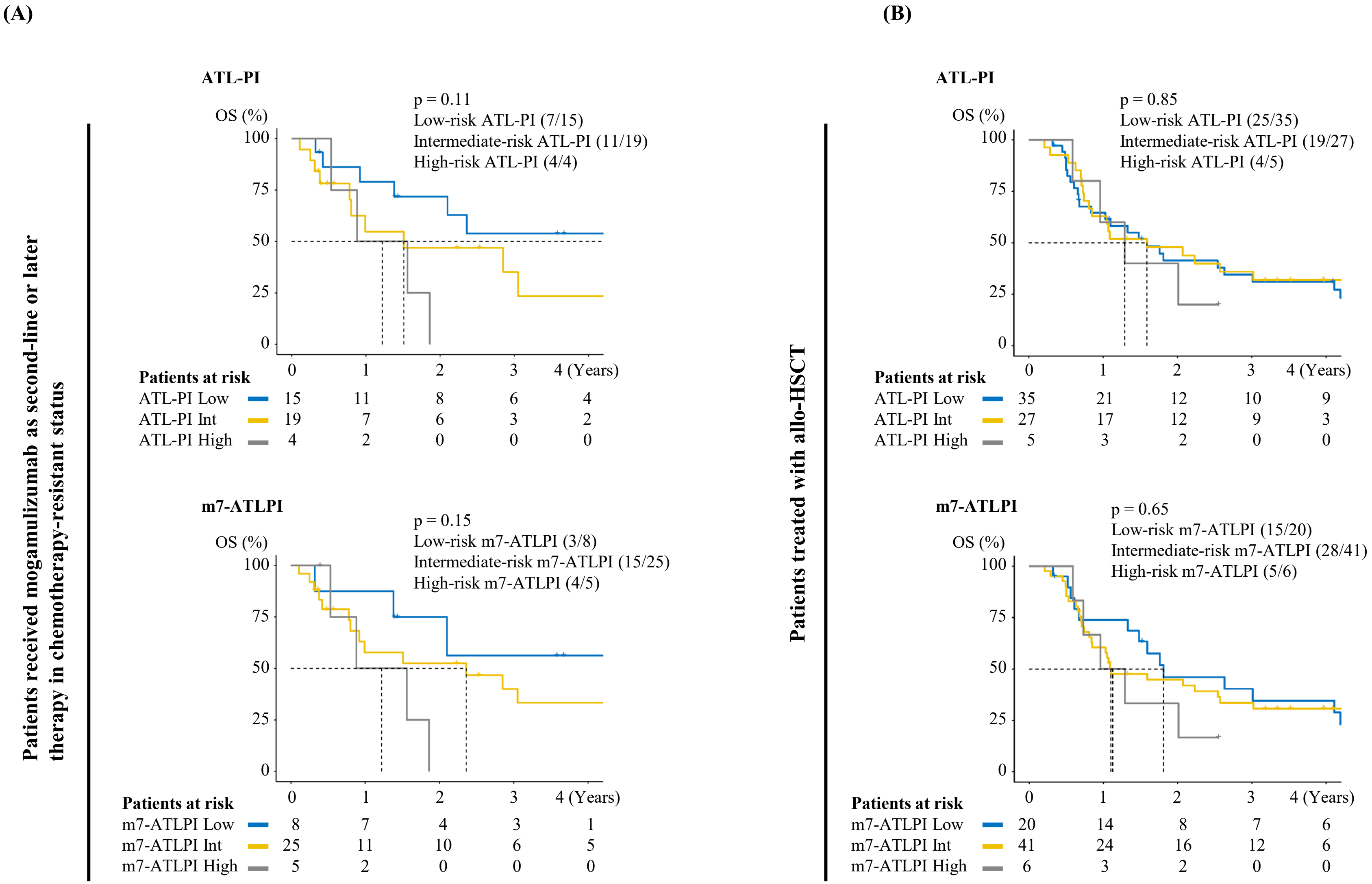
Supplemental Figure 11. Kaplan-Meier OS curves according to the ATL-PI and m7-ATLPI.

(A) Kaplan-Meier OS curves according to the ATL-PI and m7-ATLPI for the entire cohort (n = 183). Patients were not censored when they underwent allo-HSCT or mogamulizumab therapy.

(B) Kaplan-Meier OS curves according to the ATL-PI and m7-ATLPI for the entire cohort, excluding patients treated with allo-HSCT (n = 116). Patients were not censored when they underwent mogamulizumab therapy.

(C) Kaplan-Meier OS curves according to the ATL-PI and m7-ATLPI for the entire cohort, excluding patients who received allo-HSCT or mogamulizumab therapy (n = 85). Numbers in parentheses indicate the number of patients with events / number of patients per cohort.

Supplemental Figure 12



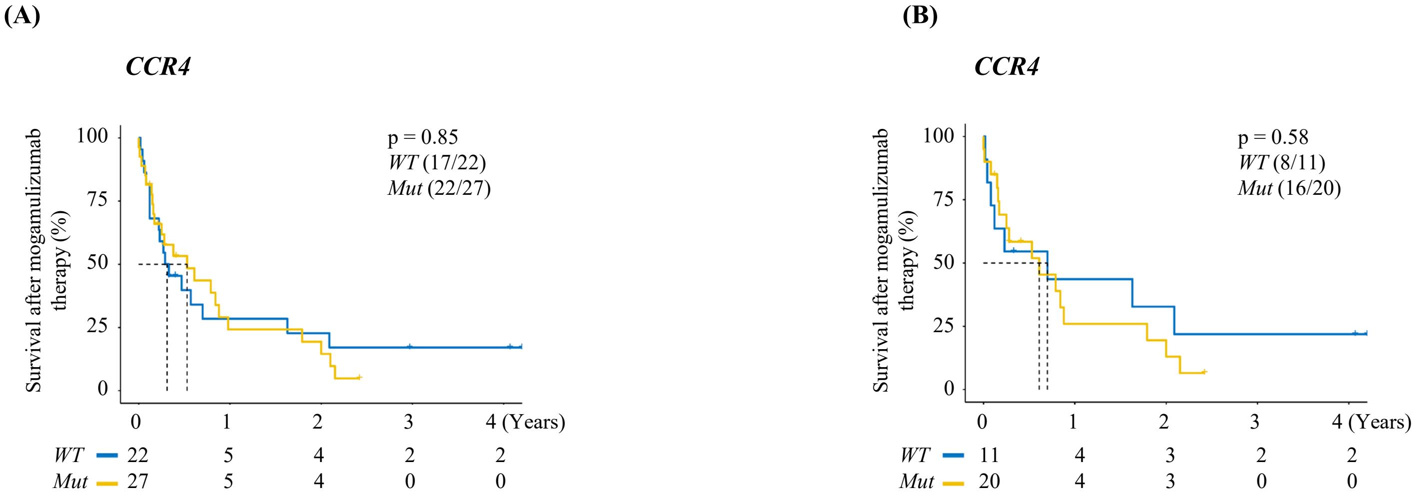
Supplemental Figure 12. Kaplan-Meier OS curves according to the ATL-PI or m7-ATLPI for patients who received immunochemotherapy (A) or allo-HSCT (B).

(A) Among patients in the entire cohort, 38 received mogamulizumab as second-line or later therapy in chemotherapy-resistant status. Survival curves of the 38 patients are shown using survival data from the date of diagnosis. There was no difference between the ATL-PI and m7-ATLPI stratification, and the m7-ATLPI could not identify those with favorable risk. In this analysis, patients were censored on the date of allo-HSCT but not on the date of mogamulizumab administration.

(B) In the entire cohort, 67 patients underwent allo-HSCT. There was no difference between the ATL-PI and m7-ATLPI stratification of these patients, and m7-ATLPI could not identify those with favorable risk. In this analysis, patients were not censored on the date of allo-HSCT or on the date of mogamulizumab administration.

Numbers on Kaplan-Meier OS curves indicate number of patients with events / number of patients per cohort.

Supplemental Figure 13



Supplemental Figure 13. Kaplan-Meier survival curves after mogamulizumab therapy according to *CCR4* mutation status in patients in the entire cohort treated with immunochemotherapy.

(A) Survival curves after mogamulizumab therapy according to *CCR4* mutation status are shown for patients in the entire cohort treated with mogamulizumab (n = 49).

(B) Survival curves after mogamulizumab therapy according to *CCR4* mutation status for patients in the entire cohort treated with mogamulizumab but without allo-HSCT (n = 31). *WT*, *wild type*; *Mut*, *mutated*.

Numbers on Kaplan-Meier OS curves indicate number of patients with events / number of patients per cohort.

Supplemental Reference

1. WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues: Adult T-cell leukaemia/lymphoma (ed. by Swerdlow, S.H. et al.). IARC press Lyon:281-84, 2008
2. Tsukasaki K, Hermine O, Bazarbachi A, et al: Definition, prognostic factors, treatment, and response criteria of adult T-cell leukemia-lymphoma: a proposal from an international consensus meeting. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 27:453-9, 2009
3. Kataoka K, Iwanaga M, Yasunaga JI, et al: Prognostic relevance of integrated genetic profiling in adult T-cell leukemia/lymphoma. Blood 131:215-225, 2018
4. Kataoka K, Nagata Y, Kitanaka A, et al: Integrated molecular analysis of adult T cell leukemia/lymphoma. Nat Genet 47:1304-15, 2015
5. Zou H, Hastie T: Regularization and Variable Selection via the Elastic Net. Journal of the Royal Statistical Society. Series B (Statistical Methodology) 67:301-320, 2005
6. Nagata Y, Kontani K, Enami T, et al: Variegated RHOA mutations in adult T-cell leukemia/lymphoma. Blood 127:596-604, 2016