JUNB, DUSP2, SGK1, SOCS1 and CREBBP are frequently mutated in T-cell/histiocyte-rich large B-cell lymphoma

Bianca Schuhmacher,[1] Julia Bein,[1] Tobias Rausch,[2,3] Vladimir Benes,[2] Thomas Tousseyn,[4] Martine Vornanen,[5] Maurilio Ponzoni,[6] Lorenz Thurner,[7,8] Randy Gascoyne,[9] Christian Steidl,[9] Ralf Küppers,[10,11] Martin-Leo Hansmann[1,12,13] and Sylvia Hartmann[1,12]

[1]Dr. Senckenberg Institute of Pathology, Goethe University, Frankfurt am Main, Germany; [2]Genecore, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany; [3]Genome Biology Unit, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany; [4]Department of Pathology, University Hospitals K.U.Leuven, Belgium; [5]Department of Pathology, Tampere University Hospital and University of Tampere, Finland; [6]Unit of Lymphoid Malignancies, Department of Pathology, Scientific Institute San Raffaele, Milan, Italy; [7]José Carreras Center for Immuno and Gene Therapy and Internal Medicine I, Saarland University Medical School, Homburg, Saar, Germany; [8]Department of Internal Medicine 2, Hospital of the J. W. Goethe University, Frankfurt am Main, Germany; [9]Department of Pathology and Laboratory Medicine and the Centre for Lymphoid Cancer, British Columbia Cancer Agency, University of British Columbia, Vancouver, Canada; [10]Institute of Cell Biology (Cancer Research), Faculty of Medicine, University of Duisburg-Essen, Essen, Germany; [11]Deutsches Konsortium für Translationale Krebsforschung (DKTK), Germany; [12]Reference and Consultant Center for Lymphoma and Lymph Node Diagnostics, Goethe University, Frankfurt am Main, Germany and [13]Frankfurt Institute of Advanced Studies, Frankfurt am Main, Germany

Supplementary Methods

PCR amplification of target genes and validation of mutations by Sanger sequencing

Pools of 20 microdissected cells were incubated with 0.25 mg/ml proteinase K (Roche) for 3 h at 55°C followed by heat inactivation of the enzyme for 5 min at 95°C. For validation of selected mutations, microdissected tumor and non-tumor cells were applied in a two-rounded seminested PCR. In the first round of amplification, five to six primer pairs (each primer at 0.1 µM final concentration) per case were multiplexed in a 50 µl reaction using the Expand High Fidelity PCR System (Roche). The cycling program consisted of an initial denaturation step at 95°C for 5 min, followed by 35 cycles of 95°C for 30 sec, an annealing temperature of 59°C or 61°C for 30 sec and 72°C for 1 min, followed by a final incubation at 72°C for 10 min. In the second round of PCR (40 cycles), 2 µl aliquots of the first round of PCR were used as template to amplify separate products in a 30 µl reaction using Taq DNA polymerase (Thermo Scientific, Dreieich, Germany). PCR products ranging from 250 - 400 bp in size were analyzed on a 2% agarose gel, purified from the PCR reaction mixture using the innuPREP DOUBLEpure Kit (Analytik Jena, Jena, Germany) and subjected to Sanger sequencing (Eurofins Genomics, Ebersberg, Germany). Primer sequences are provided in Supplementary Table S5.

Analysis of SHM motifs

The CCDS of genes of interest was analyzed for the presence of SHM hotspot motifs (WRCY/RGYW) using the A plasmid Editor (ApE) software tool. The mutation frequency at SHM hotspot sites expected by chance and observed in the CDS of each gene were calculated and then compared by the X^2-test, adopted from Mottok *et al.*[1] The mutation frequency expected to occur within SHM hotspot by chance is represented by the ratio of cytosines/guanines within the motifs (WRCY/RGYW), only counting cytosines/guanines on position three/two, and cytosines/guanines outside SHM motifs, also including cytosines/guanines on position four/one of the motifs. The observed frequency was calculated by the respective ratio of nonsynonymous (Supplementary Table S3) and synonymous (Supplementary Table S4) mutations detected within SHM motifs and found outside the motifs. Additional criteria indicating aberrant SHM activity including the the ratio

1

of mutations at C:G sites to A:T sites and the ratio of transitions to transversions were investigated similarly.

Supplementary Tables

Supplementary Table S1. Genes selected for targeted resequencing of NLPHL and THRLBCL cases.

Supplementary Table S2. Coverages of targeted resequencing.

Supplementary Table S3. Nonsynonymous SNVs identified by targeted resequencing in NLPHL and THRLBCL cohorts.

Supplementary Table S4. Synonymous SNVs in the seven most recurrently mutated genes identified by targeted resequencing in NLPHL and THRLBCL cohorts.

Supplementary Table S5. Sequences of oligonucleotides used for validation of selected mutations in a two round seminested PCR.

Supplementary References

1. Mottok A, Woolcock B, Chan FC, et al. Genomic Alterations in CIITA Are Frequent in Primary Mediastinal Large B Cell Lymphoma and Are Associated with Diminished MHC Class II Expression. Cell Rep 2015;13(7):1418–1431.

Supplementary Table S1. Genes selected for targeted resequencing of NLPHL and THRLBCL cases.

Gene

ATM	MYO1A
BASP1	NES
BCL6	NFATC3
BCOR	NOTCH3
CASP9	NPAT
COL25A1	NSD1
COL4A1	NUP188
CREBBP	PARP14
CRTC2	PDGFRB
DLG1	PGAM2
DUSP1	PTPN1
DUSP2	RBM47
EIF3A	REPS1
EP300	RUSC1
FN1	SDF4
GABRP	SGK1
GLO1	SMAD6
HELLS	SOCS1
HHEX	STXBP5
HIST1H3G	SV2B
IFT172	TBK1
ITGA2	TCEB3
JAK2	TIMM9
JUNB	TMPRSS9
KL	TRRAP
KLHL6	UMPS
KYNU	XYLT1
LHCGR	ZNF141
LYPLAL1	ZNF273
MMP1	ZNF281
MPP1	ZNF564

Supplementary Table S2. Coverages of targeted resequencing.

Case	On Target Percentage	Average Target Coverage
1	76	4723.92
2	77	5278.78
3	76	4370.22
4	75	4067.02
5	76	4144.88
6	74	3481.98
7	75	4057.16
8	75	4257.4
9	76	4730.23
10	76	4539.03
11	76	4063.5
12	76	4386.77
13	77	4086.24
14	77	4761.37
15	75	4122.54
16	79	7814.66
17	79	5178.93
18	79	4783.04
19	80	7282.51
20	79	5563.68
21	78	7736.71
22	81	4807.89
23	79	7604.39
24	81	4632.55
25	78	8488.89
26	80	8433.24

Supplementary Table S3. Nonsynonymous SNVs identified by targeted resequencing in THRLBCL and NLPHL cohorts.

Tested and confirmed by Sanger	Case number	Diagnosis	Chromosome	Start	End	Ref	Obs	Func	Gene	Exonic Function	Amino Acid Change	Coverage	Variant Allele Frequency
	1	THRLBCL	chr11	108165730	108165730	G	A	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon32:c.G4853A:p.R1618Q	10008	0.0138
	1	THRLBCL	chr11	108154956	108154956	C	A	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon26:c.C3749A:p.S1250Y	3815	0.0110
	1	THRLBCL	chr1	15844676	15844676	C	T	exonic	CASP9	nonsynonymous SNV	CASP9:NM_001229:exon2:c.G347A:p.R116H,CASP9:NM_032996:exon2:c.G98A:p.R33H	7885	0.0082
	1	THRLBCL	chr3	196842809	196842809	G	T	exonic	DLG1	nonsynonymous SNV	DLG1:NM_001204387:exon9:c.C1183A:p.R395S,DLG1:NM_001204388:exon9:c.C1183A:p.R395S,DLG1:NM_001204386:exon13:c.C1432A:p.R478S,DLG1:NM_001098424:exon14:c.C1531A:p.R511S,DLG1:NM_004087:exon14:c.C1531A:p.R511S	4613	0.0178
	1	THRLBCL	chr10	120833357	120833357	C	A	exonic	EIF3A	stopgain SNV	EIF3A:NM_003750:exon2:c.G142T:p.E48X	3859	0.0111
	1	THRLBCL	chr10	120796711	120796711	C	T	exonic	EIF3A	nonsynonymous SNV	EIF3A:NM_003750:exon21:c.G3839A:p.R1280Q	6650	0.0030
	1	THRLBCL	chr2	216295571	216295571	C	A	exonic	FN1	nonsynonymous SNV	FN1:NM_002026:exon5:c.G552T:p.E184D,FN1:NM_054034:exon5:c.G552T:p.E184D,FN1:NM_212474:exon5:c.G552T:p.E184D,FN1:NM_212476:exon5:c.G552T:p.E184D,FN1:NM_212478:exon5:c.G552T:p.E184D,FN1:NM_212482:exon5:c.G552T:p.E184D	6807	0.0166
	1	THRLBCL	chr2	216274397	216274397	C	T	exonic	FN1	nonsynonymous SNV	FN1:NM_002026:exon15:c.G2188A:p.E730K,FN1:NM_212474:exon15:c.G2188A:p.E730K,FN1:NM_212476:exon15:c.G2188A:p.E730K,FN1:NM_212478:exon15:c.G2188A:p.E730K,FN1:NM_212482:exon15:c.G2188A:p.E730K	10448	0.0162
	1	THRLBCL	chr2	216274346	216274346	C	T	exonic	FN1	nonsynonymous SNV	FN1:NM_002026:exon15:c.G2239A:p.V747M,FN1:NM_212474:exon15:c.G2239A:p.V747M,FN1:NM_212476:exon15:c.G2239A:p.V747M,FN1:NM_212478:exon15:c.G2239A:p.V747M,FN1:NM_212482:exon15:c.G2239A:p.V747M	7141	0.0147

1	THRLBCL	chr2	216236704	216236704	C	T	exonic	FN1	stopgain SNV	FN1:NM_212474:exon38:c.G5739A:p.W1913X,FN1:NM_212476:exon38:c.G6099A:p.W2033X,FN1:NM_002026:exon40:c.G6276A:p.W2092X,FN1:NM_212478:exon40:c.G6201A:p.W2067X,FN1:NM_212482:exon40:c.G6642A:p.W2214X	2724	0.0055
1	THRLBCL	chr10	96350213	96350213	G	A	exonic	HELLS	nonsynonymous SNV	HELLS:NM_018063:exon14:c.G1532A:p.R511Q	4844	0.0184
1	THRLBCL	chr6	26271235	26271235	C	G	exonic	HIST1H3G	nonsynonymous SNV	HIST1H3G:NM_003534:exon1:c.G378C:p.Q126H	5454	0.0145
1	THRLBCL	chr2	27706523	27706523	G	A	exonic	IFT172	nonsynonymous SNV	IFT172:NM_015662:exon6:c.C406T:p.R136C	7922	0.0194
1	THRLBCL	chr2	27706186	27706186	G	T	exonic	IFT172	nonsynonymous SNV	IFT172:NM_015662:exon7:c.C540A:p.F180L	2766	0.0145
1	THRLBCL	chr9	5126730	5126730	G	A	exonic	JAK2	nonsynonymous SNV	JAK2:NM_004972:exon25:c.G3338A:p.R1113H	8615	0.0181
1	THRLBCL	chr19	12902979	12902979	C	T	exonic	JUNB	stopgain SNV	JUNB:NM_002229:exon1:c.C394T:p.Q132X	4403	0.0186
1	THRLBCL	chr3	183273303	183273303	C	T	exonic	KLHL6	nonsynonymous SNV	KLHL6:NM_130446:exon1:c.G139A:p.V47I	6350	0.0033
1	THRLBCL	chr1	156641102	156641102	C	A	exonic	NES	stopgain SNV	NES:NM_006617:exon4:c.G2878T:p.E960X	13223	0.0203
1	THRLBCL	chr19	15296413	15296413	T	G	exonic	NOTCH3	nonsynonymous SNV	NOTCH3:NM_000435:exon13:c.A2029C:p.N677H	10840	0.0131
1	THRLBCL	chr5	176562844	176562844	G	A	exonic	NSD1	nonsynonymous SNV	NSD1:NM_022455:exon2:c.G740A:p.S247N	6866	0.0079
1	THRLBCL	chr5	176562133	176562133	G	T	exonic	NSD1	nonsynonymous SNV	NSD1:NM_022455:exon2:c.G29T:p.R10I	14396	0.0167
1	THRLBCL	chr9	131767427	131767427	T	C	exonic	NUP188	nonsynonymous SNV	NUP188:NM_015354:exon39:c.T4436C:p.V1479A	13069	0.0168
1	THRLBCL	chr20	49181570	49181570	A	C	exonic	PTPN1	nonsynonymous SNV	PTPN1:NM_002827:exon3:c.A219C:p.K73N	11560	0.0168
1	THRLBCL	chr16	11349047	11349047	G	A	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C289T:p.P97S	7713	0.0156
1	THRLBCL	chr16	11349026	11349026	G	A	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C310T:p.R104C	7764	0.0160
1	THRLBCL	chr16	11348908	11348908	C	T	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G428A:p.S143N	2192	0.0219
1	THRLBCL	chr6	147525676	147525676	A	C	exonic	STXBP5	nonsynonymous SNV	STXBP5:NM_001127715:exon1:c.A8C:p.K3T,STXBP5:NM_139244:exon1:c.A8C:p.K3T	7904	0.0154
1	THRLBCL	chr7	98575894	98575894	G	A	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_003496:exon55:c.G8371A:p.A2791T,TRRAP:NM_001244580:exon56:c.G8425A:p.A2809T	7512	0.0141

	1	THRLBCL	chr7	98529178	98529178	G	A	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_001244580:exon26:c.G3742A:p.E1248K,TRRAP:NM_003496:exon26:c.G3742A:p.E1248K	9173	0.0162
	1	THRLBCL	chr7	64388903	64388903	G	T	exonic	ZNF273	nonsynonymous SNV	ZNF273:NM_021148:exon4:c.G1197T:p.E399D	1632	0.0123
	2	THRLBCL	chr3	196842808	196842808	C	T	exonic	DLG1	nonsynonymous SNV	DLG1:NM_001204387:exon9:c.G1184A:p.R395H,DLG1:NM_001204388:exon9:c.G1184A:p.R395H,DLG1:NM_001204386:exon13:c.G1433A:p.R478H,DLG1:NM_001098424:exon14:c.G1532A:p.R511H,DLG1:NM_004087:exon14:c.G1532A:p.R511H	5772	0.0035
yes	2	THRLBCL	chr2	96810609	96810609	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G401A:p.G134D	18793	0.0122
yes	2	THRLBCL	chr2	96809901	96809901	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon3:c.G722A:p.G241D	6972	0.0086
yes	2	THRLBCL	chr19	12902600	12902600	G	A	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.G15A:p.M5I	6718	0.0086
	2	THRLBCL	chr20	49127128	49127128	G	A	splicing	PTPN1(NM_002827:exon1:c.63+1G>A)			13059	0.0116
yes	2	THRLBCL	chr6	134492840	134492840	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon9:c.C901T:p.P301S,SGK1:NM_001143678:exon9:c.C859T:p.P287S,SGK1:NM_005627:exon9:c.C817T:p.P273S,SGK1:NM_001143676:exon11:c.C1102T:p.P368S	12246	0.0171
yes	2	THRLBCL	chr6	134492803	134492803	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon9:c.C938G:p.A313G,SGK1:NM_001143678:exon9:c.C896G:p.A299G,SGK1:NM_005627:exon9:c.C854G:p.A285G,SGK1:NM_001143676:exon11:c.C1139G:p.A380G	4388	0.0089
	2	THRLBCL	chr6	134498923	134498923	C	T	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon1:c.G38A:p.S13N	7502	0.0053
	2	THRLBCL	chr6	134495912	134495912	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_005627:exon1:c.C34T:p.L12F	1606	0.0100
	2	THRLBCL	chr6	134494411	134494411	C	G	splicing	SGK1(NM_005627:exon6:c.417+1G>C,NM_001143678:exon6:c.459+1(			7955	0.0147
yes	2	THRLBCL	chr16	11348951	11348951	G	A	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C385T:p.H129Y	1273	0.0126
yes	2	THRLBCL	chr16	11348945	11348945	G	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C391G:p.Q131E	2003	0.0075
yes	2	THRLBCL	chr16	11348923	11348923	T	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.A413C:p.D138A	2679	0.0056
yes	2	THRLBCL	chr16	11348912	11348912	C	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G424C:p.E142Q	2725	0.0055
yes	2	THRLBCL	chr16	11348902	11348902	T	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.A434G:p.D145G	3860	0.0073

3	THRLBCL	chrX	39913233	39913233	C	T	exonic	BCOR	nonsynonymous SNV	BCOR:NM_001123384:exon13:c.G4726A:p.D1576N,BCOR:NM_001123383:exon14:c.G4780A:p.D1594N,BCOR:NM_001123385:exon14:c.G4882A:p.D1628N,BCOR:NM_017745:exon14:c.G4780A:p.D1594N	13157	0.0177
3	THRLBCL	chr16	3790454	3790454	C	G	exonic	CREBBP	nonsynonymous SNV	CREBBP:NM_001079846:exon23:c.G3965C:p.R1322P,CREBBP:NM_004380:exon24:c.G4079C:p.R1360P	13954	0.0162
3	THRLBCL	chr3	196846291	196846291	C	A	exonic	DLG1	stopgain SNV	DLG1:NM_001204387:exon8:c.G1027T:p.E343X,DLG1:NM_001204388:exon8:c.G1027T:p.E343X,DLG1:NM_001204386:exon12:c.G1276T:p.E426X,DLG1:NM_001098424:exon13:c.G1375T:p.E459X,DLG1:NM_004087:exon13:c.G1375T:p.E459X	3008	0.0160
3	THRLBCL	chr3	196842829	196842829	C	G	exonic	DLG1	nonsynonymous SNV	DLG1:NM_001204387:exon9:c.G1163C:p.G388A,DLG1:NM_001204388:exon9:c.G1163C:p.G388A,DLG1:NM_001204386:exon13:c.G1412C:p.G471A,DLG1:NM_001098424:exon14:c.G1511C:p.G504A,DLG1:NM_004087:exon14:c.G1511C:p.G504A	3986	0.0120
3	THRLBCL	chr6	26271433	26271433	C	G	exonic	HIST1H3G	nonsynonymous SNV	HIST1H3G:NM_003534:exon1:c.G180C:p.E60D	13432	0.0134
3	THRLBCL	chr19	12902731	12902731	G	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.G146C:p.S49T	3266	0.0122
3	THRLBCL	chr19	12902640	12902640	G	T	exonic	JUNB	stopgain SNV	JUNB:NM_002229:exon1:c.G55T:p.G19X	4855	0.0138
3	THRLBCL	chr19	15297788	15297788	C	T	exonic	NOTCH3	nonsynonymous SNV	NOTCH3:NM_000435:exon12:c.G1852A:p.E618K	8890	0.0025
3	THRLBCL	chr19	15290025	15290025	G	T	exonic	NOTCH3	nonsynonymous SNV	NOTCH3:NM_000435:exon22:c.C3529A:p.L1177I	7409	0.0038
3	THRLBCL	chr1	155291644	155291644	C	T	exonic	RUSC1	nonsynonymous SNV	RUSC1:NM_001105203:exon2:c.C80T:p.S27F,RUSC1:NM_001105204:exon2:c.C80T:p.S27F	1031	0.0175
3	THRLBCL	chr6	134494626	134494626	C	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon4:c.G391C:p.V131L,SGK1:NM_001143678:exon4:c.G349C:p.V117L,SGK1:NM_005627:exon4:c.G307C:p.V103L,SGK1:NM_001143676:exon6:c.G592C:p.V198L	5188	0.0085

3	THRLBCL	chr6	134495666	134495666	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon2:c.C219G:p.N73K,SGK1:NM_001143678:exon2:c.C177G:p.N59K,SGK1:NM_005627:exon2:c.C135G:p.N45K,SGK1:NM_001143676:exon4:c.C420G:p.N140K	4417	0.0057
3	THRLBCL	chr6	134496681	134496681	C	T	splicing	SGK1(NM_001143678:exon2:c.118+1G>A)			4269	0.0045
3	THRLBCL	chr16	11348951	11348951	G	A	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C385T:p.H129Y	825	0.0267
3	THRLBCL	chr16	11348945	11348945	G	A	exonic	SOCS1	stopgain SNV	SOCS1:NM_003745:exon2:c.C391T:p.Q131X	1451	0.0110
3	THRLBCL	chr16	11349301	11349301	G	A	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C35T:p.A12V	6816	0.0164
3	THRLBCL	chr16	11348978	11348978	C	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G358C:p.A120P	3421	0.0050
3	THRLBCL	chr16	11348949	11348949	G	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C387G:p.H129Q	827	0.0157
3	THRLBCL	chr16	11348907	11348907	G	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C429G:p.S143R	2057	0.0092
3	THRLBCL	chr12	64878147	64878147	A	G	exonic	TBK1	nonsynonymous SNV	TBK1:NM_013254:exon9:c.A1057G:p.I353V	6447	0.0095
4	THRLBCL	chr5	17275524	17275524	G	A	exonic	BASP1	nonsynonymous SNV	BASP1:NM_001271606:exon2:c.G199A:p.E67K,BASP1:NM_006317:exon2:c.G199A:p.E67K	4977	0.0032
4	THRLBCL	chr16	3900392	3900392	G	A	exonic	CREBBP	nonsynonymous SNV	CREBBP:NM_001079846:exon2:c.C704T:p.S235L,CREBBP:NM_004380:exon2:c.C704T:p.S235L	6649	0.0029
4	THRLBCL	chr6	147685192	147685192	C	T	exonic	STXBP5	nonsynonymous SNV	STXBP5:NM_139244:exon23:c.C2863T:p.R955W,STXBP5:NM_001127715:exon25:c.C2971T:p.R991W	6843	0.0031
4	THRLBCL	chr16	17294394	17294394	C	T	exonic	XYLT1	nonsynonymous SNV	XYLT1:NM_022166:exon4:c.G1031A:p.R344H	3006	0.0047
5	THRLBCL	chr2	96810528	96810528	G	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.C482A:p.S161Y	6936	0.0027
5	THRLBCL	chr19	12902730	12902730	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A145G:p.S49G	4821	0.0046
5	THRLBCL	chr19	12902713	12902713	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T128C:p.L43P	5455	0.0042
5	THRLBCL	chr19	12902707	12902707	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T122C:p.V41A	5456	0.0033
5	THRLBCL	chr19	12902617	12902617	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A32G:p.H11R	8843	0.0040
5	THRLBCL	chr19	12902610	12902610	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T25C:p.F9L	8781	0.0028
5	THRLBCL	chr5	149511610	149511610	C	A	exonic	PDGFRB	nonsynonymous SNV	PDGFRB:NM_002609:exon8:c.G1175T:p.G392V	1601	0.0062

	5	THRLBCL	chr16	11349333	11349333	C	T	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G3A:p.M1I	6381	0.0045
	5	THRLBCL	chr16	11349318	11349318	C	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G18C:p.Q6H	6454	0.0042
	5	THRLBCL	chr16	11349317	11349317	C	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G19C:p.V7L	6462	0.0042
	5	THRLBCL	chr16	11349310	11349310	G	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C26G:p.A9G	6379	0.0042
	5	THRLBCL	chr16	11349262	11349262	G	T	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C74A:p.P25H	5976	0.0032
	6	THRLBCL	chr2	216262402	216262402	C	T	splicing	FN1(NM_002026:exon23:c.3517+1G>A,NM_212474:exon23:c.3517+1(		4586	0.0035
	6	THRLBCL	chr1	1154308	1154308	C	A	splicing	SDF4(NM_016547:exon6:c.578-1G>T,NM_016176:exon6:c.578-1G>T)		3519	0.0040
yes	7	THRLBCL	chr2	96810600	96810600	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G410A:p.G137D	13028	0.0031
yes	7	THRLBCL	chr2	96810597	96810597	C	A	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G413T:p.C138F	12559	0.0134
yes	7	THRLBCL	chr2	96810517	96810517	C	A	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G493T:p.A165S	8190	0.0121
yes	7	THRLBCL	chr2	96810085	96810085	G	C	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon3:c.C538G:p.L180V	5712	0.0168
yes	7	THRLBCL	chr2	96810072	96810072	C	G	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon3:c.G551C:p.S184T	3421	0.0050
yes	7	THRLBCL	chr2	96809966	96809966	G	C	exonic	DUSP2	stopgain SNV	DUSP2:NM_004418:exon3:c.C657G:p.Y219X	6000	0.0173
	7	THRLBCL	chr2	96810613	96810613	C	G	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G397C:p.D133H	13312	0.0134
	7	THRLBCL	chr2	96809739	96809739	G	C	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon4:c.C768G:p.H256Q	7815	0.0096
	7	THRLBCL	chr6	26271396	26271396	G	C	exonic	HIST1H3G	nonsynonymous SNV	HIST1H3G:NM_003534:exon1:c.C217G:p.R73G	19417	0.0129
yes	7	THRLBCL	chr19	12903210	12903210	C	A	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.C625A:p.P209T	3360	0.0292
yes	7	THRLBCL	chr19	12903146	12903146	C	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.C561G:p.S187R	4373	0.0151
yes	7	THRLBCL	chr19	12902634	12902634	G	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.G49C:p.A17P	4679	0.0265
yes	7	THRLBCL	chr6	134495673	134495673	G	T	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon2:c.C212A:p.A71D,SGK1:NM_001143678:exon2:c.C170A:p.A57D,SGK1:NM_005627:exon2:c.C128A:p.A43D,SGK1:NM_001143676:exon4:c.C413A:p.A138D	3336	0.0120

yes	7	THRLBCL	chr6	134495666	134495666	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon2:c.C219G:p.N73K,SGK1:NM_001143678:exon2:c.C177G:p.N59K,SGK1:NM_005627:exon2:c.C135G:p.N45K,SGK1:NM_001143676:exon4:c.C420G:p.N140K	3367	0.0113
yes	7	THRLBCL	chr6	134494288	134494288	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon6:c.A506G:p.K169R,SGK1:NM_001143678:exon6:c.A464G:p.K155R,SGK1:NM_005627:exon6:c.A422G:p.K141R,SGK1:NM_001143676:exon8:c.A707G:p.K236R	4495	0.0053
yes	7	THRLBCL	chr6	134494216	134494216	G	T	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon6:c.C578A:p.S193Y,SGK1:NM_001143678:exon6:c.C536A:p.S179Y,SGK1:NM_005627:exon6:c.C494A:p.S165Y,SGK1:NM_001143676:exon8:c.C779A:p.S260Y	5506	0.0033
yes	7	THRLBCL	chr6	134494207	134494207	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon6:c.C587G:p.T196S,SGK1:NM_001143678:exon6:c.C545G:p.T182S,SGK1:NM_005627:exon6:c.C503G:p.T168S,SGK1:NM_001143676:exon8:c.C788G:p.T263S	5530	0.0159
yes	7	THRLBCL	chr6	134493825	134493825	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon7:c.C721G:p.L241V,SGK1:NM_001143678:exon7:c.C679G:p.L227V,SGK1:NM_005627:exon7:c.C637G:p.L213V,SGK1:NM_001143676:exon9:c.C922G:p.L308V	1765	0.0074
	7	THRLBCL	chr6	134493799	134493799	C	G	splicing	SGK1(NM_005627:exon8:c.662+1G>C,NM_001143678:exon8:c.704+1(			4381	0.0157
yes	7	THRLBCL	chr7	98497371	98497371	C	T	exonic	TRRAP	stopgain SNV	TRRAP:NM_001244580:exon10:c.C781T:p.Q261X,TRRAP:NM_003496:exon10:c.C781T:p.Q261X	6129	0.0077
	7	THRLBCL	chr1	200378772	200378772	C	T	exonic	ZNF281	nonsynonymous SNV	ZNF281:NM_012482:exon2:c.G62A:p.G21D	1526	0.0085
	7	THRLBCL	chr1	200378470	200378470	G	A	exonic	ZNF281	stopgain SNV	ZNF281:NM_012482:exon2:c.C364T:p.Q122X	10122	0.0139
	7	THRLBCL	chr1	200378226	200378226	G	C	exonic	ZNF281	nonsynonymous SNV	ZNF281:NM_012482:exon2:c.C608G:p.T203S	11699	0.0132
	7	THRLBCL	chr1	200378070	200378070	G	T	exonic	ZNF281	nonsynonymous SNV	ZNF281:NM_012482:exon2:c.C764A:p.S255Y	5869	0.0097
	7	THRLBCL	chr1	200377953	200377953	C	A	exonic	ZNF281	nonsynonymous SNV	ZNF281:NM_012482:exon2:c.G881T:p.C294F	10061	0.0150
	7	THRLBCL	chr1	200377856	200377856	A	T	exonic	ZNF281	nonsynonymous SNV	ZNF281:NM_012482:exon2:c.T978A:p.F326L	11204	0.0087

8	THRLBCL	chrX	39933189	39933189	C	G	exonic	BCOR	nonsynonymous SNV	BCOR:NM_001123383:exon4:c.G1410C:p.R470S,BCOR:NM_001123384:exon4:c.G1410C:p.R470S,BCOR:NM_001123385:exon4:c.G1410C:p.R470S,BCOR:NM_017745:exon4:c.G1410C:p.R470S	5777	0.0061
8	THRLBCL	chr16	3779445	3779445	C	T	exonic	CREBBP	nonsynonymous SNV	CREBBP:NM_001079846:exon30:c.G5489A:p.R1830Q,CREBBP:NM_004380:exon31:c.G5603A:p.R1868Q	4274	0.0035
9	THRLBCL	chr1	156646901	156646901	C	T	exonic	NES	stopgain SNV	NES:NM_006617:exon1:c.G156A:p.W52X	6292	0.0030
9	THRLBCL	chr7	98524926	98524926	G	A	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_001244580:exon23:c.G3112A:p.A1038T,TRRAP:NM_003496:exon23:c.G3112A:p.A1038T	11239	0.0269
10	NLPHL pattern E	chr3	187447633	187447633	C	A	exonic	BCL6	nonsynonymous SNV	BCL6:NM_001134738:exon4:c.G560T:p.G187V,BCL6:NM_001130845:exon5:c.G560T:p.G187V,BCL6:NM_001706:exon5:c.G560T:p.G187V	1245	0.0088
10	NLPHL pattern E	chr16	3778285	3778285	G	A	exonic	CREBBP	nonsynonymous SNV	CREBBP:NM_001079846:exon30:c.C6649T:p.P2217S,CREBBP:NM_004380:exon31:c.C6763T:p.P2255S	1076	0.0130
10	NLPHL pattern E	chr5	172197691	172197691	G	A	exonic	DUSP1	nonsynonymous SNV	DUSP1:NM_004417:exon1:c.C265T:p.R89C	649	0.0154
10	NLPHL pattern E	chr2	96810517	96810517	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G493A:p.A165T	6816	0.0031
10	NLPHL pattern E	chr2	96810559	96810559	G	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.C451A:p.L151M	8690	0.0029
10	NLPHL pattern E	chr2	96810556	96810556	G	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.C454A:p.P152T	8650	0.0028
10	NLPHL pattern E	chr2	96810500	96810500	C	G	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G510C:p.Q170H	6172	0.0034
10	NLPHL pattern E	chrX	154014579	154014579	G	T	exonic	MPP1	nonsynonymous SNV	MPP1:NM_001166460:exon6:c.C526A:p.Q176K,MPP1:NM_001166461:exon6:c.C517A:p.Q173K,MPP1:NM_002436:exon6:c.C577A:p.Q193K,MPP1:NM_001166462:exon7:c.C487A:p.Q163K	7948	0.0025
10	NLPHL pattern E	chr3	122419839	122419839	G	A	exonic	PARP14	nonsynonymous SNV	PARP14:NM_017554:exon6:c.G2438A:p.R813Q	11089	0.0023
10	NLPHL pattern E	chr1	1153977	1153977	A	T	exonic	SDF4	nonsynonymous SNV	SDF4:NM_016176:exon6:c.T773A:p.F258Y,SDF4:NM_016547:exon6:c.T773A:p.F258Y	18446	0.0039
10	NLPHL pattern E	chr16	11348827	11348827	C	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.G509C:p.R170P	4364	0.0041
11	NLPHL pattern E	chr7	98553784	98553784	C	T	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_003496:exon40:c.C5878T:p.R1960W,TRRAP:NM_001244580:exon41:c.C5932T:p.R1978W	13141	0.0024

12	NLPHL pattern E	chr4	109745257	109745257	C	G	exonic	COL25A1	nonsynonymous SNV	COL25A1:NM_001256074:exon32:c.G1927C:p.D643H,COL25A1:NM_032518:exon34:c.G1918C:p.D640H	2746	0.0044
12	NLPHL pattern E	chr13	110831348	110831348	C	G	exonic	COL4A1	nonsynonymous SNV	COL4A1:NM_001845:exon31:c.G2380C:p.G794R	7703	0.0026
12	NLPHL pattern E	chr16	3830755	3830755	G	A	exonic	CREBBP	nonsynonymous SNV	CREBBP:NM_001079846:exon7:c.C1687T:p.R563W,CREBBP:NM_004380:exon8:c.C1801T:p.R601W	4876	0.0100
12	NLPHL pattern E	chr2	96810972	96810972	C	A	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon1:c.G122T:p.R41L	433	0.0185
12	NLPHL pattern E	chr22	41566474	41566474	C	T	exonic	EP300	nonsynonymous SNV	EP300:NM_001429:exon27:c.C4351T:p.H1451Y	2672	0.0348
12	NLPHL pattern E	chr2	216232745	216232745	C	T	exonic	FN1	nonsynonymous SNV	FN1:NM_212474:exon40:c.G5956A:p.E1986K,FN1:NM_212476:exon40:c.G6316A:p.E2106K,FN1:NM_002026:exon42:c.G6493A:p.E2165K,FN1:NM_212478:exon42:c.G6418A:p.E2140K,FN1:NM_212482:exon42:c.G6859A:p.E2287K	5455	0.0031
12	NLPHL pattern E	chr19	15303259	15303259	C	T	exonic	NOTCH3	nonsynonymous SNV	NOTCH3:NM_000435:exon3:c.G269A:p.R90H	5470	0.0033
12	NLPHL pattern E	chr19	15295153	15295153	C	T	exonic	NOTCH3	nonsynonymous SNV	NOTCH3:NM_000435:exon16:c.G2519A:p.G840E	5916	0.0037
13	NLPHL pattern E	chr15	91801786	91801786	T	C	splicing	SV2B(NM_001167580:exon4:c.465+2T>C,NM_014848:exon6:c.918+2T			14408	0.0025
13	NLPHL pattern E	chr7	98522767	98522767	C	A	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_001244580:exon22:c.C2856A:p.S952R,TRRAP:NM_003496:exon22:c.C2856A:p.S952R	9303	0.0029
13	NLPHL pattern E	chr4	367142	367142	A	G	exonic	ZNF141	nonsynonymous SNV	ZNF141:NM_003441:exon4:c.A916G:p.T306A	3871	0.0036
14	NLPHL pattern E	chr2	96810582	96810582	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G428A:p.C143Y	12043	0.0023
14	NLPHL pattern E	chr22	41551083	41551083	G	A	exonic	EP300	nonsynonymous SNV	EP300:NM_001429:exon17:c.G3227A:p.R1076H	9899	0.0023
14	NLPHL pattern E	chr2	27685629	27685629	C	T	exonic	IFT172	nonsynonymous SNV	IFT172:NM_015662:exon20:c.G2054A:p.R685Q	7508	0.0032
14	NLPHL pattern E	chr5	149511596	149511596	G	A	exonic	PDGFRB	nonsynonymous SNV	PDGFRB:NM_002609:exon8:c.C1189T:p.R397W	3948	0.0035
14	NLPHL pattern E	chr4	40440298	40440298	G	A	exonic	RBM47	nonsynonymous SNV	RBM47:NM_019027:exon3:c.C613T:p.R205C,RBM47:NM_001098634:exon4:c.C613T:p.R205C	6505	0.0031
14	NLPHL pattern E	chr16	11349145	11349145	T	G	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.A191C:p.Y64S	14924	0.0025
14	NLPHL pattern E	chr16	11349135	11349135	G	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C201G:p.I67M	14943	0.0024

14	NLPHL pattern E	chr12	64868056	64868056	A	C	exonic	TBK1	nonsynonymous SNV	TBK1:NM_013254:exon6:c.A587C:p.K196T	2908	0.0055
15	NLPHL pattern E	chrX	39933184	39933184	C	A	exonic	BCOR	nonsynonymous SNV	BCOR:NM_001123383:exon4:c.G1415T:p.G472V,BCOR:NM_001123384:exon4:c.G1415T:p.G472V,BCOR:NM_001123385:exon4:c.G1415T:p.G472V,BCOR:NM_017745:exon4:c.G1415T:p.G472V	3772	0.0045
15	NLPHL pattern E	chr16	3790512	3790512	G	A	exonic	CREBBP	stopgain SNV	CREBBP:NM_001079846:exon23:c.C3907T:p.R1303X,CREBBP:NM_004380:exon24:c.C4021T:p.R1341X	9391	0.0029
15	NLPHL pattern E	chr2	216284010	216284010	G	A	exonic	FN1	nonsynonymous SNV	FN1:NM_002026:exon12:c.C1774T:p.R592C,FN1:NM_054034:exon12:c.C1774T:p.R592C,FN1:NM_212474:exon12:c.C1774T:p.R592C,FN1:NM_212476:exon12:c.C1774T:p.R592C,FN1:NM_212478:exon12:c.C1774T:p.R592C,FN1:NM_212482:exon12:c.C1774T:p.R592C	2779	0.0047
15	NLPHL pattern E	chr5	176637294	176637294	C	T	exonic	NSD1	stopgain SNV	NSD1:NM_022455:exon5:c.C1894T:p.R632X,NSD1:NM_172349:exon6:c.C1087T:p.R363X	13865	0.0021
16	NLPHL pattern A	chr2	96810760	96810760	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon1:c.G334A:p.A112T	5900	0.0031
16	NLPHL pattern A	chr2	96810739	96810739	G	A	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon1:c.C355T:p.R119C	9095	0.0029
16	NLPHL pattern A	chr2	96810724	96810724	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon1:c.G370A:p.A124T	10799	0.0031
16	NLPHL pattern A	chr2	27676363	27676363	A	C	exonic	IFT172	nonsynonymous SNV	IFT172:NM_015662:exon35:c.T3839G:p.V1280G	4870	0.0037
16	NLPHL pattern A	chr19	12902719	12902719	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A134G:p.D45G	4848	0.0033
16	NLPHL pattern A	chr19	12902715	12902715	G	A	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.G130A:p.A44T	5137	0.0033
16	NLPHL pattern A	chr3	183209938	183209938	C	T	exonic	KLHL6	nonsynonymous SNV	KLHL6:NM_130446:exon7:c.G1643A:p.R548Q	3953	0.0053
17	NLPHL pattern A	chr4	109861750	109861750	C	A	exonic	COL25A1	nonsynonymous SNV	COL25A1:NM_001256074:exon8:c.G605T:p.R202I,COL25A1:NM_032518:exon9:c.G617T:p.R206I,COL25A1:NM_198721:exon9:c.G617T:p.R206I	4232	0.0085
17	NLPHL pattern A	chr3	122411370	122411370	T	C	exonic	PARP14	nonsynonymous SNV	PARP14:NM_017554:exon4:c.T578C:p.V193A	8799	0.0026
17	NLPHL pattern A	chr19	2422230	2422230	C	A	exonic	TMPRSS9	nonsynonymous SNV	TMPRSS9:NM_182973:exon13:c.C2431A:p.H811N	2704	0.0067

18	NLPHL pattern A	chrX	39911598	39911598	G	A	exonic	BCOR	nonsynonymous SNV	BCOR:NM_001123384:exon14:c.C4876T:p.R1626C,BCOR:NM_001123383:exon15:c.C4930T:p.R1644C,BCOR:NM_001123385:exon15:c.C5032T:p.R1678C,BCOR:NM_017745:exon15:c.C4930T:p.R1644C	811	0.0123
18	NLPHL pattern A	chr1	153920595	153920595	C	T	exonic	CRTC2	nonsynonymous SNV	CRTC2:NM_181715:exon14:c.G2072A:p.R691Q	7509	0.0028
18	NLPHL pattern A	chr2	96809761	96809761	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon4:c.G746A:p.S249N	18274	0.0030
18	NLPHL pattern A	chr5	170222251	170222251	G	T	exonic	GABRP	nonsynonymous SNV	GABRP:NM_014211:exon5:c.G280T:p.D94Y	2798	0.0043
18	NLPHL pattern A	chr6	38652177	38652177	G	T	exonic	GLO1	nonsynonymous SNV	GLO1:NM_006708:exon3:c.C281A:p.S94Y	3837	0.0039
18	NLPHL pattern A	chr5	52322598	52322598	G	T	exonic	ITGA2	nonsynonymous SNV	ITGA2:NM_002203:exon2:c.G85T:p.A29S	5401	0.0044
18	NLPHL pattern A	chr3	183211979	183211979	C	A	exonic	KLHL6	nonsynonymous SNV	KLHL6:NM_130446:exon5:c.G1238T:p.R413M	5586	0.0039
18	NLPHL pattern A	chr16	68225040	68225040	C	A	exonic	NFATC3	nonsynonymous SNV	NFATC3:NM_004555:exon9:c.C2468A:p.S823Y,NFATC3:NM_173163:exon9:c.C2468A:p.S823Y,NFATC3:NM_173165:exon9:c.C2468A:p.S823Y	5429	0.0041
18	NLPHL pattern A	chr5	176638477	176638477	C	A	exonic	NSD1	nonsynonymous SNV	NSD1:NM_022455:exon5:c.C3077A:p.P1026H,NSD1:NM_172349:exon6:c.C2270A:p.P757H	3734	0.0043
18	NLPHL pattern A	chr5	176562179	176562179	T	C	exonic	NSD1	nonsynonymous SNV	NSD1:NM_172349:exon2:c.T8C:p.L3P	9916	0.0027
18	NLPHL pattern A	chr3	122418741	122418741	T	C	exonic	PARP14	nonsynonymous SNV	PARP14:NM_017554:exon6:c.T1340C:p.V447A	8086	0.0054
18	NLPHL pattern A	chr16	17352959	17352959	C	A	exonic	XYLT1	nonsynonymous SNV	XYLT1:NM_022166:exon3:c.G799T:p.A267S	5480	0.0033
18	NLPHL pattern A	chr1	200377294	200377294	T	C	exonic	ZNF281	nonsynonymous SNV	ZNF281:NM_012482:exon2:c.A1540G:p.I514V	7109	0.0032
18	NLPHL pattern A	chr19	12637636	12637636	G	A	exonic	ZNF564	nonsynonymous SNV	ZNF564:NM_144976:exon4:c.C1286T:p.A429V	3047	0.0056
19	NLPHL pattern A	chr22	41527619	41527619	C	T	exonic	EP300	nonsynonymous SNV	EP300:NM_001429:exon6:c.C1510T:p.R504W	13832	0.0029
19	NLPHL pattern A	chr19	12637637	12637637	C	A	exonic	ZNF564	nonsynonymous SNV	ZNF564:NM_144976:exon4:c.G1285T:p.A429S	9876	0.0025
20	NLPHL pattern A	chr5	17275698	17275698	G	T	exonic	BASP1	nonsynonymous SNV	BASP1:NM_001271606:exon2:c.G373T:p.A125S,BASP1:NM_006317:exon2:c.G373T:p.A125S	4575	0.0033
20	NLPHL pattern A	chr13	110814619	110814619	G	T	exonic	COL4A1	nonsynonymous SNV	COL4A1:NM_001845:exon48:c.C4420A:p.L1474I	10307	0.0026

20	NLPHL pattern A	chr16	3778366	3778366	G	C	exonic	CREBBP	nonsynonymous SNV	CREBBP:NM_001079846:exon30:c.C6568G:p.H2190D,CREBBP:NM_004380:exon31:c.C6682G:p.H2228D	3963	0.0035
20	NLPHL pattern A	chr2	216230304	216230304	G	C	exonic	FN1	nonsynonymous SNV	FN1:NM_212474:exon41:c.C6165G:p.D2055E,FN1:NM_212476:exon41:c.C6525G:p.D2175E,FN1:NM_002026:exon43:c.C6702G:p.D2234E,FN1:NM_212478:exon43:c.C6627G:p.D2209E,FN1:NM_212482:exon43:c.C7068G:p.D2356E	7505	0.0068
20	NLPHL pattern A	chr2	27706220	27706220	G	T	exonic	IFT172	nonsynonymous SNV	IFT172:NM_015662:exon7:c.C506A:p.S169Y	5779	0.0031
20	NLPHL pattern A	chr15	91825067	91825067	G	T	exonic	SV2B	stopgain SNV	SV2B:NM_001167580:exon9:c.G1030T:p.E344X,SV2B:NM_014848:exon11:c.G1483T:p.E495X	6044	0.0033
20	NLPHL pattern A	chr19	2422116	2422116	A	C	exonic	TMPRSS9	nonsynonymous SNV	TMPRSS9:NM_182973:exon13:c.A2317C:p.T773P	5672	0.0041
21	NLPHL pattern B	chr6	134496682	134496682	C	T	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.G118A:p.A40T	9176	0.0033
21	NLPHL pattern B	chr6	134495169	134495169	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon3:c.C286T:p.L96F,SGK1:NM_001143678:exon3:c.C244T:p.L82F,SGK1:NM_005627:exon3:c.C202T:p.L68F,SGK1:NM_001143676:exon5:c.C487T:p.L163F	25269	0.0026
21	NLPHL pattern B	chr6	134492804	134492804	C	T	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon9:c.G937A:p.A313T,SGK1:NM_001143678:exon9:c.G895A:p.A299T,SGK1:NM_005627:exon9:c.G853A:p.A285T,SGK1:NM_001143676:exon11:c.G1138A:p.A380T	6906	0.0049
21	NLPHL pattern B	chr6	134491533	134491533	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon12:c.C1253T:p.T418I,SGK1:NM_001143678:exon12:c.C1211T:p.T404I,SGK1:NM_005627:exon12:c.C1169T:p.T390I,SGK1:NM_001143676:exon14:c.C1454T:p.T485I	15722	0.0031
21	NLPHL pattern B	chr19	2418125	2418125	G	A	exonic	TMPRSS9	nonsynonymous SNV	TMPRSS9:NM_182973:exon12:c.G2041A:p.D681N	5963	0.0032
21	NLPHL pattern B	chr7	98515280	98515280	C	A	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_001244580:exon20:c.C2600A:p.P867Q,TRRAP:NM_003496:exon20:c.C2600A:p.P867Q	1388	0.0072
21	NLPHL pattern B	chr7	98515267	98515267	G	A	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_001244580:exon20:c.G2587A:p.D863N,TRRAP:NM_003496:exon20:c.G2587A:p.D863N	1282	0.0094
22	NLPHL pattern D	chr10	120820320	120820320	G	T	exonic	EIF3A	nonsynonymous SNV	EIF3A:NM_003750:exon9:c.C1264A:p.P422T	4871	0.0037

22	NLPHL pattern D	chr10	120817578	120817578	G	A	exonic	EIF3A	nonsynonymous SNV	EIF3A:NM_003750:exon12:c.C1867T:p.R623C	6707	0.0091
22	NLPHL pattern D	chr10	120801566	120801566	G	A	exonic	EIF3A	nonsynonymous SNV	EIF3A:NM_003750:exon19:c.C3466T:p.R1156W	14074	0.0026
22	NLPHL pattern D	chr22	41562617	41562617	G	T	exonic	EP300	nonsynonymous SNV	EP300:NM_001429:exon23:c.G3821T:p.G1274V	4223	0.0036
22	NLPHL pattern D	chr2	216262496	216262496	C	A	exonic	FN1	nonsynonymous SNV	FN1:NM_002026:exon22:c.G3424T:p.G1142C,FN1:NM_212474:exon22:c.G3424T:p.G1142C,FN1:NM_212476:exon22:c.G3424T:p.G1142C,FN1:NM_212478:exon22:c.G3424T:p.G1142C,FN1:NM_212482:exon22:c.G3424T:p.G1142C	6889	0.0033
22	NLPHL pattern D	chr5	52351438	52351438	G	A	exonic	ITGA2	nonsynonymous SNV	ITGA2:NM_002203:exon8:c.G850A:p.G284S	3414	0.0044
22	NLPHL pattern D	chr1	156641939	156641939	G	T	exonic	NES	nonsynonymous SNV	NES:NM_006617:exon4:c.C2041A:p.P681T	6266	0.0032
22	NLPHL pattern D	chr11	108040717	108040717	C	A	exonic	NPAT	nonsynonymous SNV	NPAT:NM_002519:exon14:c.G2839T:p.G947W	9101	0.0025
22	NLPHL pattern D	chr9	131763817	131763817	C	A	exonic	NUP188	nonsynonymous SNV	NUP188:NM_015354:exon35:c.C3853A:p.L1285M	7649	0.0029
22	NLPHL pattern D	chr6	134638590	134638590	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143676:exon1:c.C9G:p.N3K	5725	0.0031
22	NLPHL pattern D	chr6	134496744	134496744	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.C56T:p.P19L	816	0.0294
22	NLPHL pattern D	chr6	134494244	134494244	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon6:c.C550G:p.H184D,SGK1:NM_001143678:exon6:c.C508G:p.H170D,SGK1:NM_005627:exon6:c.C466G:p.H156D,SGK1:NM_001143676:exon8:c.C751G:p.H251D	8804	0.0031
22	NLPHL pattern D	chr15	91795630	91795630	T	C	exonic	SV2B	nonsynonymous SNV	SV2B:NM_001167580:exon3:c.T211C:p.Y71H,SV2B:NM_014848:exon5:c.T664C:p.Y222H	6507	0.0106
22	NLPHL pattern D	chr16	17353351	17353351	C	A	exonic	XYLT1	nonsynonymous SNV	XYLT1:NM_022166:exon3:c.G407T:p.G136V	7028	0.0034
22	NLPHL pattern D	chr7	64388091	64388091	C	A	exonic	ZNF273	nonsynonymous SNV	ZNF273:NM_021148:exon4:c.C385A:p.Q129K	5552	0.0031
23	NLPHL pattern C	chr11	108114820	108114820	T	C	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon6:c.T637C:p.F213L	21059	0.0045
23	NLPHL pattern C	chr11	108114817	108114817	T	C	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon6:c.T634C:p.F212L	21028	0.0057
23	NLPHL pattern C	chr11	108114773	108114773	G	A	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon6:c.G590A:p.G197E	17062	0.0026
23	NLPHL pattern C	chr11	108114770	108114770	A	G	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon6:c.A587G:p.K196R	17196	0.0025

		23	NLPHL pattern C	chr11	108114751	108114751	A	G	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon6:c.A568G:p.I190V	18425	0.0037
		23	NLPHL pattern C	chr11	108114728	108114728	T	C	exonic	ATM	nonsynonymous SNV	ATM:NM_000051:exon6:c.T545C:p.V182A	19412	0.0074
		23	NLPHL pattern C	chr2	96810618	96810618	C	A	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G392T:p.G131V	21340	0.0033
		23	NLPHL pattern C	chr19	12902736	12902736	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A151G:p.K51E	8977	0.0028
		23	NLPHL pattern C	chr19	12902734	12902734	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T149C:p.L50P	8672	0.0025
		23	NLPHL pattern C	chr19	12902709	12902709	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A124G:p.N42D	9140	0.0072
		23	NLPHL pattern C	chr19	12902686	12902686	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T101C:p.L34P	7610	0.0030
		23	NLPHL pattern C	chr19	12902683	12902683	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A98G:p.K33R	7854	0.0028
		23	NLPHL pattern C	chr19	12902674	12902674	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A89G:p.H30R	7000	0.0029
		23	NLPHL pattern C	chr19	12902671	12902671	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T86C:p.L29P	15010	0.0039
		23	NLPHL pattern C	chr19	12902611	12902611	T	C	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.T26C:p.F9S	17062	0.0032
		23	NLPHL pattern C	chr19	12902586	12902586	A	G	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.A1G:p.M1V	11419	0.0032
		23	NLPHL pattern C	chr6	134498954	134498954	A	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon1:c.T7C:p.S3P	39241	0.0033
		23	NLPHL pattern C	chr6	134498948	134498948	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon1:c.A13G:p.S5G	37904	0.0026
		23	NLPHL pattern C	chr6	134498927	134498927	A	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon1:c.T34C:p.C12R	21709	0.0032
		23	NLPHL pattern C	chr6	134498917	134498917	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon1:c.A44G:p.E15G	18312	0.0028
		24	NLPHL pattern C	chr22	41523536	41523536	C	A	exonic	EP300	nonsynonymous SNV	EP300:NM_001429:exon4:c.C952A:p.P318T	6967	0.0027
		24	NLPHL pattern C	chr2	216284020	216284020	G	T	exonic	FN1	stopgain SNV	FN1:NM_002026:exon12:c.C1764A:p.Y588X,FN1:NM_054034:exon12:c.C1764A:p.Y588X,FN1:NM_212474:exon12:c.C1764A:p.Y588X,FN1:NM_212476:exon12:c.C1764A:p.Y588X,FN1:NM_212478:exon12:c.C1764A:p.Y588X,FN1:NM_212482:exon12:c.C1764A:p.Y588X	5591	0.0030
		24	NLPHL pattern C	chr19	12902918	12902918	C	A	exonic	JUNB	stopgain SNV	JUNB:NM_002229:exon1:c.C333A:p.Y111X	2555	0.0055
		24	NLPHL pattern C	chr19	2425145	2425145	C	A	exonic	TMPRSS9	nonsynonymous SNV	TMPRSS9:NM_182973:exon15:c.C2761A:p.L921M	2962	0.0047

24	NLPHL pattern C	chr7	98564676	98564676	C	T	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_003496:exon48:c.C7114T:p.R2372W,TRRAP:NM_001244580:exon49:c.C7168T:p.R2390W	7534	0.0033
24	NLPHL pattern C	chr7	98490104	98490104	C	T	exonic	TRRAP	nonsynonymous SNV	TRRAP:NM_001244580:exon5:c.C319T:p.R107C,TRRAP:NM_003496:exon5:c.C319T:p.R107C	2439	0.0049
25	NLPHL pattern D	chr19	12903112	12903112	C	T	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.C527T:p.P176L	7672	0.0030
25	NLPHL pattern D	chr19	12902869	12902869	G	A	exonic	JUNB	nonsynonymous SNV	JUNB:NM_002229:exon1:c.G284A:p.S95N	8421	0.0030
25	NLPHL pattern D	chr9	131752504	131752504	C	T	exonic	NUP188	nonsynonymous SNV	NUP188:NM_015354:exon25:c.C2639T:p.T880M	21305	0.0026
25	NLPHL pattern D	chr6	134496762	134496762	A	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.T38C:p.L13P	8690	0.0028
25	NLPHL pattern D	chr6	134496753	134496753	A	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.T47C:p.L16P	6062	0.0040
25	NLPHL pattern D	chr6	134496748	134496748	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.C52T:p.R18W	5100	0.0051
25	NLPHL pattern D	chr6	134496738	134496738	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.A62G:p.H21R	4506	0.0036
25	NLPHL pattern D	chr6	134496732	134496732	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.A68G:p.K23R	4611	0.0043
25	NLPHL pattern D	chr6	134496712	134496712	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.A88G:p.R30G	31880	0.0039
25	NLPHL pattern D	chr6	134496709	134496709	T	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.A91G:p.S31G	31725	0.0037
25	NLPHL pattern D	chr6	134496699	134496699	A	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143678:exon1:c.T101C:p.F34S	29110	0.0027
26	NLPHL pattern D	chr13	110839601	110839601	G	A	exonic	COL4A1	nonsynonymous SNV	COL4A1:NM_001845:exon25:c.C1612T:p.R538W	23871	0.0028
26	NLPHL pattern D	chr2	96810517	96810517	C	A	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G493T:p.A165S	10555	0.0029
26	NLPHL pattern D	chr2	96810531	96810531	C	T	exonic	DUSP2	nonsynonymous SNV	DUSP2:NM_004418:exon2:c.G479A:p.R160H	10464	0.0034
26	NLPHL pattern D	chr2	27688716	27688716	T	C	exonic	IFT172	nonsynonymous SNV	IFT172:NM_015662:exon17:c.A1726G:p.K576E	3809	0.0037
26	NLPHL pattern D	chr19	12902601	12902601	G	T	exonic	JUNB	stopgain SNV	JUNB:NM_002229:exon1:c.G16T:p.E6X	9150	0.0034
26	NLPHL pattern D	chr6	134494655	134494655	G	A	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon4:c.C362T:p.A121V,SGK1:NM_001143678:exon4:c.C320T:p.A107V,SGK1:NM_005627:exon4:c.C278T:p.A93V,SGK1:NM_001143676:exon6:c.C563T:p.A188V	5447	0.0039

26	NLPHL pattern D	chr6	134494619	134494619	C	T	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon4:c.G398A:p.G133E,SGK1:NM_001143678:exon4:c.G356A:p.G119E,SGK1:NM_005627:exon4:c.G314A:p.G105E,SGK1:NM_001143676:exon6:c.G599A:p.G200E	13019	0.0035
26	NLPHL pattern D	chr6	134494418	134494418	C	G	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon5:c.G495C:p.K165N,SGK1:NM_001143678:exon5:c.G453C:p.K151N,SGK1:NM_005627:exon5:c.G411C:p.K137N,SGK1:NM_001143676:exon7:c.G696C:p.K232N	10785	0.0027
26	NLPHL pattern D	chr6	134492247	134492247	G	C	exonic	SGK1	nonsynonymous SNV	SGK1:NM_001143677:exon10:c.C1036G:p.P346A,SGK1:NM_001143678:exon10:c.C994G:p.P332A,SGK1:NM_005627:exon10:c.C952G:p.P318A,SGK1:NM_001143676:exon12:c.C1237G:p.P413A	18004	0.0028
26	NLPHL pattern D	chr16	11348766	11348766	G	C	exonic	SOCS1	nonsynonymous SNV	SOCS1:NM_003745:exon2:c.C570G:p.N190K	15606	0.0027
26	NLPHL pattern D	chr7	64389297	64389297	C	T	exonic	ZNF273	stopgain SNV	ZNF273:NM_021148:exon4:c.C1591T:p.R531X	8692	0.0026

Supplementary Table S4. Synonymous SNVs in the seven most recurrently mutated genes identified by targeted resequencing in THRLBCL and NLPHL cohorts.

Case number	Diagnosis	Chr	Start	End	Ref	Obs	Func	Gene	Exonic Function	Amino Acid Change	Coverage	Variant Allele Frequency
1	THRLBCL	chr16	11349078	11349078	C	T	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.G258A:p.V86V	5014	0.0247
1	THRLBCL	chr16	11348808	11348808	C	T	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.G528A:p.E176E	3601	0.0067
2	THRLBCL	chr2	96809915	96809915	G	A	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon3:c.C708T:p.F236F	9115	0.0170
2	THRLBCL	chr2	96809766	96809766	C	T	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon4:c.G741A:p.K247K	13341	0.0143
2	THRLBCL	chr2	96809948	96809948	C	T	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon3:c.G675A:p.E225E	8670	0.0127
2	THRLBCL	chr2	96810743	96810743	C	T	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon1:c.G351A:p.E117E	6900	0.0107
2	THRLBCL	chr2	96810716	96810716	G	A	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon1:c.C378T:p.Y126Y	11997	0.0060
2	THRLBCL	chr6	134496737	134496737	G	A	exonic	SGK1	synonymous SNV	SGK1:NM_001143678:exon1:c.C63T:p.H21H	1410	0.0170
2	THRLBCL	chr6	134494176	134494176	G	A	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon6:c.C618T:p.Y206Y,SGK1:NM_001143678:exon6:c.C576T:p.Y192Y,SGK1:NM_005627:exon6:c.C534T:p.Y178Y,SGK1:NM_001143676:exon8:c.C819T:p.Y273Y	10671	0.0159
2	THRLBCL	chr16	11348889	11348889	C	T	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.G447A:p.E149E	3932	0.0074
2	THRLBCL	chr16	11349006	11349006	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C330T:p.N110N	7128	0.0069
2	THRLBCL	chr16	11348880	11348880	C	T	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.G456A:p.E152E	4389	0.0068
2	THRLBCL	chr16	11348814	11348814	C	T	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.G522A:p.L174L	4207	0.0048
2	THRLBCL	chr16	11348745	11348745	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C591T:p.N197N	10524	0.0039
2	THRLBCL	chr16	11348726	11348726	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C610T:p.L204L	11537	0.0037
3	THRLBCL	chr16	11348937	11348937	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C399T:p.G133G	2018	0.0094
4	THRLBCL	chr7	98529225	98529225	G	A	exonic	TRRAP	synonymous SNV	TRRAP:NM_001244580:exon26:c.G3789A:p.S1263S,TRRAP:NM_003496:exon26:c.G3789A:p.S1263S	2943	0.0054
5	THRLBCL	chr2	96810545	96810545	C	T	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon2:c.G465A:p.G155G	7724	0.0040
5	THRLBCL	chr2	216245694	216245694	C	T	exonic	FN1	synonymous SNV	FN1:NM_002026:exon32:c.G5001A:p.S1667S,FN1:NM_212478:exon32:c.G5001A:p.S1667S,FN1:NM_212482:exon33:c.G5274A:p.S1758S	6058	0.0031
5	THRLBCL	chr19	12903628	12903628	G	A	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.G1043A:p.X348X	6317	0.0049
5	THRLBCL	chr19	12902732	12902732	T	C	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.T147C:p.S49S	4917	0.0033
5	THRLBCL	chr19	12902591	12902591	C	T	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.C6T:p.C2C	7124	0.0028
6	THRLBCL	chr16	3779090	3779090	C	T	exonic	CREBBP	synonymous SNV	CREBBP:NM_001079846:exon30:c.G5844A:p.T1948T,CREBBP:NM_004380:exon31:c.G5958A:p.T1986T	3238	0.0043
8	THRLBCL	chr2	96810584	96810584	C	T	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon2:c.G426A:p.L142L	18133	0.0039
8	THRLBCL	chr2	96809972	96809972	G	A	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon3:c.C651T:p.F217F	9362	0.0038
8	THRLBCL	chr7	98490094	98490094	C	T	exonic	TRRAP	synonymous SNV	TRRAP:NM_001244580:exon5:c.C309T:p.N103N,TRRAP:NM_003496:exon5:c.C309T:p.N103N	1649	0.0085
10	NLPHL pattern E	chr16	11348811	11348811	C	T	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.G525A:p.Q175Q	3674	0.0049

12	NLPHL pattern E	chr2	216289821	216289821	C	T	exonic	FN1	synonymous SNV	FN1:NM_002026:exon7:c.G1032A:p.E344E,FN1:NM_054034:exon7:c.G1032A:p.E344E,FN1:NM_212474:exon7:c.G1032A:p.E344E,FN1:NM_212476:exon7:c.G1032A:p.E344E,FN1:NM_212478:exon7:c.G1032A:p.E344E,FN1:NM_212482:exon7:c.G1032A:p.E344E	2910	0.0320
12	NLPHL pattern E	chr7	98563326	98563326	C	T	exonic	TRRAP	synonymous SNV	TRRAP:NM_003496:exon47:c.C6909T:p.S2303S,TRRAP:NM_001244580:exon48:c.C6963T:p.S2321S	4665	0.0034
16	NLPHL pattern A	chr2	96810752	96810752	C	T	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon1:c.G342A:p.L114L	5469	0.0033
16	NLPHL pattern A	chr19	12902774	12902774	C	T	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.C189T:p.G63G	7065	0.0031
19	NLPHL pattern A	chr16	3779210	3779210	T	G	exonic	CREBBP	synonymous SNV	CREBBP:NM_001079846:exon30:c.A5724C:p.P1908P,CREBBP:NM_004380:exon31:c.A5838C:p.P1946P	80	0.1000
21	NLPHL pattern B	chr6	134491973	134491973	G	A	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon11:c.C1203T:p.N401N,SGK1:NM_001143678:exon11:c.C1161T:p.N387N,SGK1:NM_005627:exon11:c.C1119T:p.N373N,SGK1:NM_001143676:exon13:c.C1404T:p.N468N	3160	0.0060
21	NLPHL pattern B	chr16	11349126	11349126	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C210T:p.A70A	23059	0.0034
21	NLPHL pattern B	chr16	11349162	11349162	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C174T:p.F58F	24546	0.0033
22	NLPHL pattern D	chr2	216245721	216245721	T	C	exonic	FN1	synonymous SNV	FN1:NM_002026:exon32:c.A4974G:p.Q1658Q,FN1:NM_212478:exon32:c.A4974G:p.Q1658Q,FN1:NM_212482:exon33:c.A5247G:p.Q1749Q	17253	0.0057
23	NLPHL pattern C	chr2	96810896	96810896	A	G	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon1:c.T198C:p.V66V	170	0.0471
23	NLPHL pattern C	chr19	12902684	12902684	A	G	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.A99G:p.K33K	7602	0.0034
23	NLPHL pattern C	chr19	12902738	12902738	A	G	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.A153G:p.K51K	8923	0.0034
23	NLPHL pattern C	chr19	12902756	12902756	A	G	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.A171G:p.G57G	8827	0.0033
23	NLPHL pattern C	chr19	12902657	12902657	T	C	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.T72C:p.P24P	21898	0.0020
23	NLPHL pattern C	chr6	134498928	134498928	T	C	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon1:c.A33G:p.A11A	22425	0.0030
23	NLPHL pattern C	chr6	134498934	134498934	T	C	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon1:c.A27G:p.S9S	23270	0.0024
23	NLPHL pattern C	chr6	134495182	134495182	A	G	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon3:c.T273C:p.P91P,SGK1:NM_001143678:exon3:c.T231C:p.P77P,SGK1:NM_005627:exon3:c.T189C:p.P63P,SGK1:NM_001143676:exon5:c.T474C:p.P158P	37618	0.0021
23	NLPHL pattern C	chr6	134495199	134495199	A	G	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon3:c.T256C:p.L86L,SGK1:NM_001143678:exon3:c.T214C:p.L72L,SGK1:NM_005627:exon3:c.T172C:p.L58L,SGK1:NM_001143676:exon5:c.T457C:p.L153L	36769	0.0020
23	NLPHL pattern C	chr6	134498886	134498886	A	G	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon1:c.T75C:p.P25P	17909	0.0020

23	NLPHL pattern C	chr6	134495149	134495149	A	G	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon3:c.T306C:p.S102S,SGK1:NM_001143678:exon3:c.T264C:p.S88S,SGK1:NM_005627:exon3:c.T222C:p.S74S,SGK1:NM_001143676:exon5:c.T507C:p.S169S	45872	0.0017
24	NLPHL pattern C	chr2	216257655	216257655	C	T	exonic	FN1	synonymous SNV	FN1:NM_212482:exon25:c.G4068A:p.T1356T	7452	0.0028
24	NLPHL pattern C	chr6	134495663	134495663	G	C	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon2:c.C222G:p.S74S,SGK1:NM_001143678:exon2:c.C180G:p.S60S,SGK1:NM_005627:exon2:c.C138G:p.S46S,SGK1:NM_001143676:exon4:c.C423G:p.S141S	3905	0.0038
24	NLPHL pattern C	chr7	98515146	98515146	G	A	exonic	TRRAP	synonymous SNV	TRRAP:NM_001244580:exon20:c.G2466A:p.P822P,TRRAP:NM_003496:exon20:c.G2466A:p.P822P	18720	0.0051
25	NLPHL pattern D	chr2	96810851	96810851	G	A	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon1:c.C243T:p.V81V	402	0.0174
25	NLPHL pattern D	chr2	96810086	96810086	G	A	exonic	DUSP2	synonymous SNV	DUSP2:NM_004418:exon3:c.C537T:p.Y179Y	12408	0.0031
25	NLPHL pattern D	chr19	12903242	12903242	G	A	exonic	JUNB	synonymous SNV	JUNB:NM_002229:exon1:c.G657A:p.A219A	9970	0.0049
25	NLPHL pattern D	chr6	134496686	134496686	T	C	exonic	SGK1	synonymous SNV	SGK1:NM_001143678:exon1:c.A114G:p.G38G	26865	0.0038
25	NLPHL pattern D	chr6	134496755	134496755	G	A	exonic	SGK1	synonymous SNV	SGK1:NM_001143678:exon1:c.C45T:p.S15S	6499	0.0031
25	NLPHL pattern D	chr6	134496692	134496692	C	T	exonic	SGK1	synonymous SNV	SGK1:NM_001143678:exon1:c.G108A:p.L36L	27432	0.0022
26	NLPHL pattern D	chr6	134494260	134494260	C	G	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon6:c.G534C:p.L178L,SGK1:NM_001143678:exon6:c.G492C:p.L164L,SGK1:NM_005627:exon6:c.G450C:p.L150L,SGK1:NM_001143676:exon8:c.G735C:p.L245L	9399	0.0033
26	NLPHL pattern D	chr6	134495188	134495188	G	A	exonic	SGK1	synonymous SNV	SGK1:NM_001143677:exon3:c.C267T:p.S89S,SGK1:NM_001143678:exon3:c.C225T:p.S75S,SGK1:NM_005627:exon3:c.C183T:p.S61S,SGK1:NM_001143676:exon5:c.C468T:p.S156S	31546	0.0019
26	NLPHL pattern D	chr16	11348709	11348709	G	A	exonic	SOCS1	synonymous SNV	SOCS1:NM_003745:exon2:c.C627T:p.F209F	22815	0.0020

Supplementary Table S5. Sequences of oligonucleotides used for validation of selected mutations in a two round seminested PCR.

Case	Gene	First PCR round		Second PCR round	
		Primer	Sequence (5'-->3')	Primer	Sequence (5'-->3')
2, 7	DUSP2	DUSP2-Exon2-FW	GTACTTCCTGCGAGGTGAGCAA		
		DUSP2-Exon2-Rev1	ATGGCAGGCTCTTTCCCTAGA	DUSP2-Exon2-Rev2	TCCCTAGAGGCGCCCAGT
2	DUSP2	DUSP2-Exon3a-FW1	GGCAGAGCGCGAGATACC	DUSP2-Exon3a-FW2	TGGCAGTGCACCAGCACC
		DUSP2-Exon3a-Rev	TCCAGGGTGGCCCTGTGG		
7	DUSP2	DUSP2-Exon3b-FW1	AGTCCTCTTGTCTCGGCCA	DUSP2-Exon3b-FW2	TTGTCTCGGCCAGCCCAT
		DUSP2-Exon3b-Rev	CCCAGTCCTCTCCTCTGGA		
2,7	JUNB	JUNB-1-FW	AGGCACCCAGTCCGGT		
		JUNB-1-Rev1	ACAATCAGGCGTTCCAGCTC	JUNB-1-Rev2	AAGAGGCGAGCTTGAGAGAC
7	JUNB	JUNB-2-FW	CAAAGCCCTGGACGATCTGC		
		JUNB-2-Rev1	GTCTGCGGTTCCTCCTTGAA	JUNB-2-Rev2	CTCCTTGAAGGTGGAGGCG
2	SGK1	SGK1-Exon9-FW1	AATATGCCTCTTAGCTGCTTTTGATAAGC	SGK1-Exon9-FW2	GTACTGGTAAGGGCAAGACACC
		SGK1-Exon9-Rev	ACTAAATGTGTGGTCGTGGGATTGC		
7	SGK1	SGK1-Exon2-FW1	ATCTCCAGTTCAAGCCAAATCAGC	SGK1-Exon2-FW2	TCAAATATATTAGAATTTAAGGAGAAATGAGATCC
		SGK1-Exon2-Rev	GGACGTTATGAAGCCGTCTAAACG		
7	SGK1	SGK1-Exon6-FW1	GAGATGTGCTTGATGGGGCTG	SGK1-Exon6-FW2	CATTGGCGGTAGACACTCCT
		SGK1-Exon6-Rev	GGCTGTGCAGAGACACTAAG		
7	SGK1	SGK1-Exon7-FW1	CAAGCCAGCTCACGTGCTAGG	SGK1-Exon7-FW2	GATCTGGTTTTAGGCAACCAAGTTGC
		SGK1-Exon7-Rev	CCCAGAATGACTTTGTTCTGTCTCC		
2	SOCS1	SOCS1-3-FW1	CTGGACGCCTGCGGATTCTA	SOCS1-3-FW2	TGCGGATTCTACTGGGGGC
		SOCS1-3-Rev	AGCTCAGGTAGTCGCGGA		
7	TRRAP	TRRAP-Stop-FW1	GTGATGATTCTTCGGTATGCCAG	TRRAP-Stop-FW2	CCATAGCAGAGTGTCAATGTATGAA
		TRRAP-Stop-Rev	CCTGAAACACAGGTGCAGAAA		