SUPPLEMENTARY APPENDIX

Targeted next-generation sequencing in chronic lymphocytic leukemia: a high-throughput yet tailored approach will facilitate implementation in a clinical setting

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Supplemental Table 1. Characteristics of patients included in the study

Patients	**188**
Age at diagnosis: median, range (years)*	62 (38-85)
Gender (M/F)**	105/65
Binet stage	
A	82
B	38
C	22
NA	46
Therapy Status	
Treated	116
Untreated	29
NA	43
***IGHV* Status**	
IGHV3-21 subset #2	51
Unmutated	137
Recurrent Genomic Aberrations[#]	
del(17p)	16
del(11q)	32
trisomy 12	12
del(13q)	37
no recurrent aberration	56
NA	35

NA: not available

**data not available for 36 patients*

***data not available for 18 patients*

[#]*based on the hierarchical model of genomic subgroups*

Supplemental Table 2. Samples not fulfiling the 0.8 coverage threshold

Sample	% covered 10x	% covered 50x	% covered 100x	% covered 500x	Total mean coverage
R2_101	81	26	5	0	36,22
R2_13	96	78	58	1	145,13
R2_146	98	87	72	3	191,22
R2_34	98	90	78	37	796,4
R2_57	97	89	78	36	897,95
R2_68	96	75	52	15	235,11
R2_7	97	85	68	21	348,09
R2_78	90	62	37	1	99,27

Supplemental Table 3. Mutations detected in this study

Gene name	Position	Variant allele frequency	Read depth	Exonic type	dbSNP ID	Cosmic ID	Transcript	exon	Transcript change	AA change	Study ID
ATM	chr11:108100002	83,16	483	stopgain SNV	-	-	NM_000051	4	c.C283T	p.Q95X	R2_153
ATM	chr11:108106565	55,35	215	splice site	-	-	NM_000051	5	c.496+4T>C	-	R2_189
ATM	chr11:108115721	25,75	406	nonsynonymous SNV	-	-	NM_000051	7	c.A869T	p.H290L	R2_113
ATM	chr11:108121622	10,42	1987	nonsynonymous SNV	-	-	NM_000051	10	c.A1430G	p.K477R	R2_149
ATM	chr11:108121753	99,12	114	frameshift deletion	-	-	NM_000051	10	c.1561_1562delAG	p.R521fs	R2_191
ATM	chr11:108139203	11,22	5231	frameshift insertion	-	-	NM_000051	18	c.2705dupA	p.K902fs	R2_155
ATM	chr11:108142017	43,52	563	nonsynonymous SNV	-	-	NM_000051	20	c.T2961G	p.C987W	R2_154
ATM	chr11:108143282	40,5	279	frameshift insertion	-	-	NM_000051	21	c.3101dupA	p.Y1034fs	R2_82
ATM	chr11:108143299	50,7	856	nonsynonymous SNV	rs3092857	Yes	NM_000051	21	c.A3118G	p.M1040V	R2_105
ATM	chr11:108143545	46,67	106	stopgain SNV	-	Yes	NM_000051	22	c.C3250T	p.Q1084X	R2_41
ATM	chr11:108150225	36,78	87	stopgain SNV	-	-	NM_000051	23	c.C3292T	p.Q1098X	R2_92
ATM	chr11:108150315	27,36	899	stopgain SNV	-	Yes	NM_000051	23	c.C3382T	p.Q1128X	R2_189
ATM	chr11:108151893	16,45	1168	nonsynonymous SNV	-	-	NM_000051	24	c.A3574G	p.K1192E	R2_162
ATM	chr11:108160512	49,17	1505	nonsynonymous SNV	-	-	NM_000051	29	c.C4420G	p.H1474D	R2_169
ATM	chr11:108165784	52,05	171	frameshift deletion	-	-	NM_000051	32	c.4907delA	p.Q1636fs	R2_152
ATM	chr11:108168097	67,27	55	frameshift deletion	-	-	NM_000051	33	c.4993_4996delAAAG	p.K1665fs	R2_45
ATM	chr11:108172396	19,82	656	nonframeshift deletion	-	-	NM_000051	35	c.5199_5201delTGT	p.V1734del	R2_80
ATM	chr11:108172518	53,1	116	splice site	-	-	NM_000051	35	c.5319+2T>C	-	R2_42
ATM	chr11:108173758	41,82	112	splice site	-	-	NM_000051	36	c.5496+2T>G	-	R2_82
ATM	chr11:108175477	77,27	22	nonsynonymous SNV	-	-	NM_000051	37	c.T5572C	p.W1858R	O_5
ATM	chr11:108175528	45,14	175	stopgain SNV	-	Yes	NM_000051	37	c.C5623T	p.R1875X	R2_133
ATM	chr11:108178642	42,19	1384	nonsynonymous SNV	-	-	NM_000051	38	c.G5693A	p.R1898Q	R2_130
ATM	chr11:108186599	33,17	1658	nonsynonymous SNV	-	Yes	NM_000051	41	c.A6056G	p.Y2019C	R2_149
ATM	chr11:108196034	12,96	54	splice site	-	-	NM_000051	46	c.6573-3C>A	-	O_14
ATM	chr11:108196143	58,49	1040	nonsynonymous SNV	-	-	NM_000051	46	c.C6679T	p.R2227C	R2_87
ATM	chr11:108196954	11,36	749	splice site	-	-	NM_000051	47	c.6975+2T>C	-	R2_183
ATM	chr11:108199913	15,11	559	nonsynonymous SNV	-	-	NM_000051	49	c.A7255G	p.R2419G	R2_75
ATM	chr11:108199938	90,77	1084	nonsynonymous SNV	-	Yes	NM_000051	49	c.T7280C	p.L2427P	R2_15
ATM	chr11:108200987	49,19	124	nonsynonymous SNV	-	-	NM_000051	50	c.C7354G	p.L2452V	R2_123
ATM	chr11:108201068	29,28	997	frameshift deletion	-	-	NM_000051	50	c.7435_7438delGAAC	p.E2479fs	R2_87
ATM	chr11:108201096	37,73	327	nonsynonymous SNV	-	-	NM_000051	50	c.G7463A	p.C2488Y	R2_30
ATM	chr11:108202712	45,19	3930	nonsynonymous SNV	-	-	NM_000051	52	c.G7736C	p.R2579T	R2_153
ATM	chr11:108203578	24,61	394	frameshift deletion	-	-	NM_000051	53	c.7878_7882delTTATA	p.A2626fs	R2_30
ATM	chr11:108205735	13,16	232	stopgain SNV	-	-	NM_000051	55	c.C8050T	p.Q2684X	R2_76
ATM	chr11:108205828	10,39	552	nonsynonymous SNV	-	-	NM_000051	55	c.C8143T	p.L2715F	R2_75
ATM	chr11:108206591	24,69	738	nonsynonymous SNV	-	-	NM_000051	56	c.A8171G	p.Q2724R	R2_75
ATM	chr11:108206600	46,5	859	nonsynonymous SNV	-	-	NM_000051	56	c.T8180C	p.V2727A	R2_125
ATM	chr11:108206684	68,77	684	nonsynonymous SNV	-	-	NM_000051	56	c.A8264C	p.Y2755S	R2_40
ATM	chr11:108213995	98	550	frameshift deletion	-	-	NM_000051	57	c.8315delG	p.G2772fs	R2_185
ATM	chr11:108213997	60,63	287	frameshift insertion			NM_000051	57	c.8317_8318insCTGT	p.T2773fs	R2_61
ATM	chr11:108224493	41,17	2062	nonsynonymous SNV	-	Yes	NM_000051	60	c.G8672A	p.G2891D	R2_177
ATM	chr11:108224608	35,7	1214	splice site	rs17174393	Yes	NM_000051	60	c.8786+1G>A	-	R2_154
ATM	chr11:108235891	15,02	526	frameshift deletion	-	-	NM_000051	62	c.8933delC	p.T2978fs	R2_125

ATM	chr11:108236086	15,95	2044	nonsynonymous SNV	-	Yes	NM_000051	63	c.C9022T	p.R3008C	R2_183
ATM	chr11:108236096	83,62	7170	nonsynonymous SNV	-	Yes	NM_000051	63	c.T9032A	p.M3011K	R2_54
ATM	chr11:108236128	47,62	1267	frameshift insertion	-	-	NM_000051	63	c.9064dupG	p.E3022fs	R2_83
BIRC3	chr11:102201918	23,72	276	stopgain SNV	-	-	NM_001165	6	c.G1270T	p.E424X	R2_15
BIRC3	chr11:102201930	14,38	3014	frameshift deletion	-	-	NM_001165	6	c.1282_1285delAGGG	p.R428fs	O_4
BIRC3	chr11:102201933	23,4	599	frameshift insertion	-	-	NM_001165	6	c.1285dupG	p.E429fs	R2_17
BIRC3	chr11:102207814	10	140	nonsynonymous SNV	-	-	NM_001165	9	c.T1796G	p.V599G	R2_119
KLHL6	chr3:183245718	56,95	820	nonsynonymous SNV	-	-	NM_130446	2	c.C374T	p.T125I	R2_119
MYD88	chr3:38180226	53,95	78	nonsynonymous SNV	-	-	NM_002468	1	c.C74T	p.A25V	R2_111
MYD88	chr3:38182025	26,06	4570	nonsynonymous SNV	-	Yes	NM_002468	3	c.G649T	p.V217F	R2_5
NOTCH1	chr9:139390648	49,68	949	stopgain SNV	-	-	NM_017617	34	c.G7543T	p.E2515X	O_8
NOTCH1	chr9:139390649	48,57	1273	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	O_10
NOTCH1	chr9:139390649	22,69	221	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_103
NOTCH1	chr9:139390649	48,94	531	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_109
NOTCH1	chr9:139390649	53,13	408	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_12
NOTCH1	chr9:139390649	10,8	101	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_120
NOTCH1	chr9:139390649	19,33	119	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_130
NOTCH1	chr9:139390649	25,93	189	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_132
NOTCH1	chr9:139390649	36,43	129	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_133
NOTCH1	chr9:139390649	14,53	120	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_17
NOTCH1	chr9:139390649	14,02	970	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_180
NOTCH1	chr9:139390649	44,87	263	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_184
NOTCH1	chr9:139390649	41,33	300	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_188
NOTCH1	chr9:139390649	39,22	104	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_19
NOTCH1	chr9:139390649	56	104	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_27
NOTCH1	chr9:139390649	60	282	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_30
NOTCH1	chr9:139390649	57,14	127	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_32
NOTCH1	chr9:139390649	55,93	182	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_35
NOTCH1	chr9:139390649	50,92	168	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_44
NOTCH1	chr9:139390649	56,48	355	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_5
NOTCH1	chr9:139390649	30,86	331	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_61
NOTCH1	chr9:139390649	47,81	510	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_73
NOTCH1	chr9:139390649	42,45	509	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_82
NOTCH1	chr9:139390649	11,91	458	frameshift deletion	-	Yes	NM_017617	34	c.7541_7542delCT	p.P2514fs	R2_94
NOTCH1	chr9:139390732	33,02	848	stopgain SNV	-	-	NM_017617	34	c.C7459T	p.Q2487X	R2_124
NOTCH1	chr9:139390981	47,74	7997	stopgain SNV	-	-	NM_017617	34	c.C7210T	p.Q2404X	O_36
NOTCH1	chr9:139391014	34,78	13104	stopgain SNV	-	Yes	NM_017617	34	c.C7177T	p.Q2393X	R2_148
NOTCH1	chr9:139391053	44,3	545	nonsynonymous SNV	-	-	NM_017617	34	c.G7138A	p.V2380M	R2_102
NOTCH1	chr9:139391061	14,09	2093	nonsynonymous SNV	-	-	NM_017617	34	c.C7130T	p.P2377L	R2_18
NOTCH1	chr9:139395248	47,77	3912	nonsynonymous SNV	-	-	NM_017617	31	c.C5690T	p.T1897M	O_33
NOTCH1	chr9:139409122	47,2	1006	nonsynonymous SNV	-		NM_017617	13	c.G2047A	p.A683T	R2_58
NOTCH1	chr9:139412642	39,87	466	nonsynonymous SNV	-	-	NM_017617	7	c.C1202T	p.P401L	R2_109
NOTCH1	chr9:139413921	53,03	5383	nonsynonymous SNV	-	-	NM_017617	5	c.A839G	p.N280S	O_4
NOTCH1	chr9:139438534	10,99	91	nonsynonymous SNV	-	-	NM_017617	2	c.G82A	p.G28S	R2_45
POT1	chr7:124503411	51,7	1750	nonsynonymous SNV	-	-	NM_001042594	7	c.T146C	p.L49P	R2_5
POT1	chr7:124503666	22,76	3427	nonsynonymous SNV	-	-	NM_015450	8	c.G284T	p.G95V	R2_171
POT1	chr7:124503681	47,3	7286	nonsynonymous SNV	-	-	NM_015450	8	c.A269T	p.K90I	O_36

POT1	chr7:124511012	48,84	215	nonsynonymous SNV	-	-	NM_015450	7	c.C208T	p.P70S	R2_109
POT1	chr7:124511032	16,5	310	nonsynonymous SNV	-	-	NM_015450	7	c.G188C	p.S63T	R2_12
POT1	chr7:124532325	11,45	468	nonsynonymous SNV	-	-	NM_015450	6	c.G119A	p.G40E	R2_103
POT1	chr7:124532330	37,36	356	nonsynonymous SNV	-	-	NM_015450	6	c.C114G	p.S38R	O_7
POT1	chr7:124532331	21,99	1165	nonsynonymous SNV	-	-	NM_015450	6	c.G113A	p.S38N	R2_171
POT1	chr7:124532332	23,57	1187	nonsynonymous SNV	-	-	NM_015450	6	c.A112G	p.S38G	R2_87
POT1	chr7:124532409	12,76	243	frameshift insertion	-	-	NM_015450	6	c.34_35insTA	p.T12fs	R2_129
SF3B1	chr2:198265465	12,43	362	nonsynonymous SNV	-	-	NM_012433	18	c.T2692C	p.Y898H	O_5
SF3B1	chr2:198266482	22,98	236	nonframeshift deletion	-	Yes	NM_012433	16	c.2352_2354delGAA	p.M784_K785>I	R2_29
SF3B1	chr2:198266611	20,67	150	nonsynonymous SNV	-	Yes	NM_012433	16	c.G2225A	p.G742D	R2_110
SF3B1	chr2:198266611	15,86	2074	nonsynonymous SNV	-	Yes	NM_012433	16	c.G2225A	p.G742D	R2_148
SF3B1	chr2:198266611	17,89	693	nonsynonymous SNV	-	Yes	NM_012433	16	c.G2225A	p.G742D	R2_172
SF3B1	chr2:198266611	42,91	296	nonsynonymous SNV	-	Yes	NM_012433	16	c.G2225A	p.G742D	R2_38
SF3B1	chr2:198266611	35,94	257	nonsynonymous SNV	-	Yes	NM_012433	16	c.G2225A	p.G742D	R2_71
SF3B1	chr2:198266713	26,19	1073	nonsynonymous SNV	-	Yes	NM_012433	15	c.G2219A	p.G740E	R2_169
SF3B1	chr2:198266822	22,89	803	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2110T	p.I704F	R2_112
SF3B1	chr2:198266827	37,59	5569	frameshift deletion	-	-	NM_012433	15	c.2104_2105delCG	p.R702fs	O_2
SF3B1	chr2:198266830	36,32	1561	frameshift deletion	-	-	NM_012433	15	c.2102delT	p.V701fs	R2_178
SF3B1	chr2:198266834	28,78	4726	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	O_12
SF3B1	chr2:198266834	39,22	8000	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	O_33
SF3B1	chr2:198266834	10,64	724	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_118
SF3B1	chr2:198266834	44,52	1413	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_154
SF3B1	chr2:198266834	43,66	3209	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_155
SF3B1	chr2:198266834	14,14	4102	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_157
SF3B1	chr2:198266834	48,67	2217	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_160
SF3B1	chr2:198266834	43,68	957	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_164
SF3B1	chr2:198266834	32,14	1703	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_166
SF3B1	chr2:198266834	30,21	1731	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_168
SF3B1	chr2:198266834	23,67	1031	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_176
SF3B1	chr2:198266834	54,19	1002	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_185
SF3B1	chr2:198266834	53,96	1380	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_40
SF3B1	chr2:198266834	42,81	1185	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_47
SF3B1	chr2:198266834	40,4	4719	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_58
SF3B1	chr2:198266834	48,94	4910	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_59
SF3B1	chr2:198266834	42,37	2871	nonsynonymous SNV	-	Yes	NM_012433	15	c.A2098G	p.K700E	R2_87
SF3B1	chr2:198267369	11,34	98	nonsynonymous SNV	-	Yes	NM_012433	14	c.C1988T	p.T663I	R2_113
SF3B1	chr2:198267369	32,43	38	nonsynonymous SNV	-	Yes	NM_012433	14	c.C1988T	p.T663I	R2_24
SF3B1	chr2:198267371	32,93	164	nonsynonymous SNV	-	Yes	NM_012433	14	c.C1986A	p.H662Q	R2_174
SF3B1	chr2:198267373	20,31	262	nonsynonymous SNV	-	Yes	NM_012433	14	c.C1984G	p.H662D	R2_157
SF3B1	chr2:198267373	39,47	152	nonsynonymous SNV	-	Yes	NM_012433	14	c.C1984G	p.H662D	R2_170
SF3B1	chr2:198267383	18,12	139	nonsynonymous SNV	-	-	NM_012433	14	c.G1974C	p.W658C	R2_182
SF3B1	chr2:198267483	22,39	470	nonsynonymous SNV	-	Yes	NM_012433	14	c.G1874T	p.R625L	R2_144
SF3B1	chr2:198267489	41,5	295	nonsynonymous SNV	-	Yes	NM_012433	14	c.A1868G	p.Y623C	R2_192
SF3B1	chr2:198267489	12,15	107	nonsynonymous SNV	-	Yes	NM_012433	14	c.A1868G	p.Y623C	R2_32
SF3B1	chr2:198267491	43,75	48	nonsynonymous SNV	-	Yes	NM_012433	14	c.G1866C	p.E622D	R2_23
TP53	chr17:7576852	10,31	7573	splice site	rs11575997	Yes	NM_001126112	10	c.993+1G>T	-	O_13
TP53	chr17:7576855	73,35	2384	stopgain SNV	-	Yes	NM_001126112	9	c.C991T	p.Q331X	R2_160

TP53	chr17:7576885	80,25	1876	stopgain SNV	-	Yes	NM_001126112	9	c.A961T	p.K321X	R2_88
TP53	chr17:7577040	39,1	1404	frameshift insertion	-	-	NM_001126112	8	c.898dupC	p.P300fs	R2_129
TP53	chr17:7577094	19,97	658	nonsynonymous SNV	rs28934574	Yes	NM_001126112	8	c.C844T	p.R282W	R2_27
TP53	chr17:7577106	25,31	404	nonsynonymous SNV	-	Yes	NM_001126112	8	c.C832T	p.P278S	R2_37
TP53	chr17:7577121	21,62	7373	nonsynonymous SNV	rs121913343	Yes	NM_001126112	8	c.C817T	p.R273C	O_15
TP53	chr17:7577121	91,4	782	nonsynonymous SNV	-	Yes	NM_001126112	8	c.C817G	p.R273G	R2_85
TP53	chr17:7577538	68,26	754	nonsynonymous SNV	-	Yes	NM_001126112	7	c.G743T	p.R248L	R2_139
TP53	chr17:7577538	29,91	573	nonsynonymous SNV	rs11540652	Yes	NM_001126112	7	c.G743A	p.R248Q	R2_18
TP53	chr17:7577538	19,78	824	nonsynonymous SNV	rs11540652	Yes	NM_001126112	7	c.G743A	p.R248Q	R2_84
TP53	chr17:7577550	55,77	784	nonsynonymous SNV	-	Yes	NM_001126112	7	c.G731T	p.G244V	R2_96
TP53	chr17:7577559	27,37	813	nonsynonymous SNV	rs28934573	Yes	NM_001126112	7	c.C722T	p.S241F	R2_112
TP53	chr17:7577559	56,11	1426	nonsynonymous SNV	rs28934573	Yes	NM_001126112	7	c.C722T	p.S241F	R2_55
TP53	chr17:7577568	87,26	1369	nonsynonymous SNV	-	Yes	NM_001126112	7	c.G713A	p.C238Y	R2_93
TP53	chr17:7577570	19,06	1201	nonsynonymous SNV	-	Yes	NM_001126112	7	c.G711A	p.M237I	R2_38
TP53	chr17:7577587	27,94	1439	nonsynonymous SNV	-	Yes	NM_001126112	7	c.A694T	p.I232F	R2_123
TP53	chr17:7578271	80,93	780	nonsynonymous SNV	-	Yes	NM_001126112	6	c.A578T	p.H193L	R2_73
TP53	chr17:7578407	36,66	878	nonsynonymous SNV	rs138729528	Yes	NM_001126112	5	c.C523G	p.R175G	O_12
TP53	chr17:7578421	49,3	7600	nonsynonymous SNV	-	Yes	NM_001126112	5	c.C509T	p.T170M	R2_2
TP53	chr17:7578442	91,04	4224	nonsynonymous SNV	rs148924904	Yes	NM_001126112	5	c.A488G	p.Y163C	R2_59
TP53	chr17:7578451	30,95	4118	nonsynonymous SNV	-	Yes	NM_001126112	5	c.T479C	p.M160T	R2_117
TP53	chr17:7578461	86,03	723	nonsynonymous SNV	rs121912654	Yes	NM_001126112	5	c.G469T	p.V157F	R2_141
TP53	chr17:7578466	62,74	2411	nonsynonymous SNV	-	Yes	NM_001126112	5	c.C464T	p.T155I	R2_37
TP53	chr17:7578479	51,88	3142	frameshift insertion	-	-	NM_001126112	5	c.451dupC	p.P151fs	R2_18
TP53	chr17:7578518	18,09	4578	nonsynonymous SNV	rs28934875	Yes	NM_001126112	5	c.G412C	p.A138P	R2_19
TP53	chr17:7579366	10,76	1417	stopgain SNV	-	Yes	NM_001126112	4	c.C321G	p.Y107X	R2_4
XPO1	chr2:61719186	42,86	49	nonsynonymous SNV	-	Yes	NM_003400	16	c.A1871G	p.D624G	R2_9
XPO1	chr2:61719303	45,08	299	nonsynonymous SNV	rs79074863	Yes	NM_003400	16	c.G1754T	p.C585F	R2_19
XPO1	chr2:61719462	12,4	265	nonsynonymous SNV	-	-	NM_003400	15	c.A1721G	p.H574R	R2_72
XPO1	chr2:61719471	40,26	5567	nonsynonymous SNV	-	Yes	NM_003400	15	c.A1712T	p.E571V	O_31
XPO1	chr2:61719471	15,51	188	nonsynonymous SNV	-	-	NM_003400	15	c.A1712G	p.E571G	R2_9
XPO1	chr2:61719472	30,78	952	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	O_14
XPO1	chr2:61719472	36,39	2720	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	O_15
XPO1	chr2:61719472	39,68	3045	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	O_32
XPO1	chr2:61719472	29,43	300	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	R2_116
XPO1	chr2:61719472	31,31	923	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	R2_150
XPO1	chr2:61719472	33,69	2069	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	R2_153
XPO1	chr2:61719472	28,92	1103	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	R2_156
XPO1	chr2:61719472	43,01	641	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	R2_38
XPO1	chr2:61719472	43,25	474	nonsynonymous SNV	-	Yes	NM_003400	15	c.G1711A	p.E571K	R2_8
XPO1	chr2:61761004	46,89	2218	nonsynonymous SNV	-	-	NM_003400	2	c.A29G	p.D10G	R2_4

Supplemental Table 4. Summary of mutations and the method by which they were validated

Gene	No. of cases with mutation	No. of mutations	Mutations selected for validation	No. validated by Sanger	Mutations selected for validation	No. validated by NGS resequencing*
ATM	35	46	38	35	0	0
BIRC3	4	4	4	3	2	1
KLHL6	1	1	0	0	0	0
MYD88	2	2	2	2	0	0
NOTCH1	33	34	31	27	19	18
POT1	9	10	8	6	6	5
SF3B1	37	38	37	36	30	29
TP53	25	27	26	25	15	14
XPO1	14	15	9	9	10	10
Sum	160	177	155	143	82	77

**The entire experimental procedure was repeated for 63 of the CLL cases in order to determine the reproducibility of the targeted NGS methodology*

Supplemental Table 5. Summary of discordant mutations

Sample	Mutation found in initial NGS sequencing run	Mutation found by Sanger Sequencing	Mutation found in validation NGS sequencing run	Chr	Start	End	Reference base	Variant base	Gene	Location
R2_155	Yes	No	NA	11	108139203	108139203	-	A	ATM	exonic
R2_162	Yes	No	NA	11	108151893	108151893	A	G	ATM	exonic
R2_125	Yes	No	NA	11	108235891	108235891	C	-	ATM	exonic
R2_12	Yes	No	NA	7	124511032	124511032	C	G	POT1	exonic
R2_103	Yes	No	NA	7	124532325	124532325	C	T	POT1	exonic
R2_103	Yes	No	NA	9	139390649	139390649	CT	-	NOTCH1	exonic
R2_120	Yes	No	Yes	9	139390649	139390649	CT	-	NOTCH1	exonic
R2_132	Yes	No	Yes	9	139390649	139390649	CT	-	NOTCH1	exonic
R2_45	Yes	No	No	9	139438534	139438534	C	T	NOTCH1	exonic
R2_157	Yes	No	Yes	2	198266834	198266834	T	C	SF3B1	exonic
O_4	Yes	No	NA	11	102201930	102201933	AGGG	-	BIRC3	exonic

Sample	Type of mutation	Variant allelic ratio	No. of reads with reference	No. of reads with variant	Total reads (depth)	Transcript
R2_155	frameshift insertion	0,11	5182	586	5266	ATM:NM_000051:exon18:c.2705dupA:p.K902fs
R2_162	nonsynonymous SNV	0,16	969	191	1160	ATM:NM_000051:exon24:c.A3574G:p.K1192E
R2_125	frameshift deletion	0,15	445	79	524	ATM:NM_000051:exon62:c.8933delC:p.T2978fs
R2_12	nonsynonymous SNV	0,17	256	51	307	POT1:NM_015450:exon7:c.G188C:p.S63T
R2_103	nonsynonymous SNV	0,12	406	53	459	POT1:NM_015450:exon6:c.G119A:p.G40E
R2_103	frameshift deletion	0,23	163	49	212	NOTCH1:NM_017617:exon34:c.7541delCT:p.P2514fs
R2_120	frameshift deletion	0,12	89	11	101	NOTCH1:NM_017617:exon34:c.7541delCT:p.P2514fs
R2_132	frameshift deletion	0,27	137	50	187	NOTCH1:NM_017617:exon34:c.7541delCT:p.P2514fs
R2_45	nonsynonymous SNV	0,11	81	10	91	NOTCH1:NM_017617:exon2:c.G82A:p.G28S
R2_157	nonsynonymous SNV	0,14	3522	580	4102	SF3B1:NM_012433:exon15:c.A2098G:p.K700E
O_4	frameshift deletion	0,14	2529	432	3014	BIRC3:NM_001165:exon6:c.1282_1285delAGGG:p.R428fs

Supplemental Table 6. Small subclone detection in both the initial sequencing run and the validation sequencing run

Sample	Chr	Start	End	Reference base	Variant base	Gene	Location	Type of mutation	VAR: initial sequencing run	VAR: validation sequencing run
R2_14	17	7577114	7577114	C	A	TP53	exonic	nonsynonymous SNV	0,047142857	0,042139384
R2_14	11	102207711	102207711	G	A	BIRC3	exonic	nonsynonymous SNV	0,082026538	0,086956522
R2_34	11	102207673	102207675	AAG	-	BIRC3	exonic	nonframeshift deletion	0,023809524	0,017241379
R2_161	9	139390721	139390721	G	T	NOTCH1	exonic	stopgain SNV	0,019626168	0,030023095
R2_32	9	139391192	139391192	-	G	NOTCH1	exonic	frameshift insertion	0,054237288	0,016806723

Sample	No. of reads with reference: initial sequencing run	No. of reads with reference: validation sequencing run	No. of reads with variant: initial sequencing run	No. of reads with variant: validation sequencing run	Total reads (depth): initial sequencing run	Total reads (depth): variant sequencing run	Transcript
R2_14	667	591	33	26	700	617	TP53:NM_001126112:exon8:c.G824T:p.C275F
R2_14	761	819	68	78	829	897	BIRC3:NM_001165:exon9:c.G1693A:p.V565M
R2_34	410	114	10	2	420	116	BIRC3:NM_001165:exon9:c.1655_1657delAAG:p.E554del
R2_161	1049	420	21	13	1070	433	NOTCH1:NM_017617:exon34:c.C7470A:p.Y2490X
R2_32	283	350	16	6	299	356	NOTCH1:NM_017617:exon34:c.6999dupC:p.G2333fs

SNV: single nucleotide variant; Chr: chromosome: VAR: Variant allelic ratio