

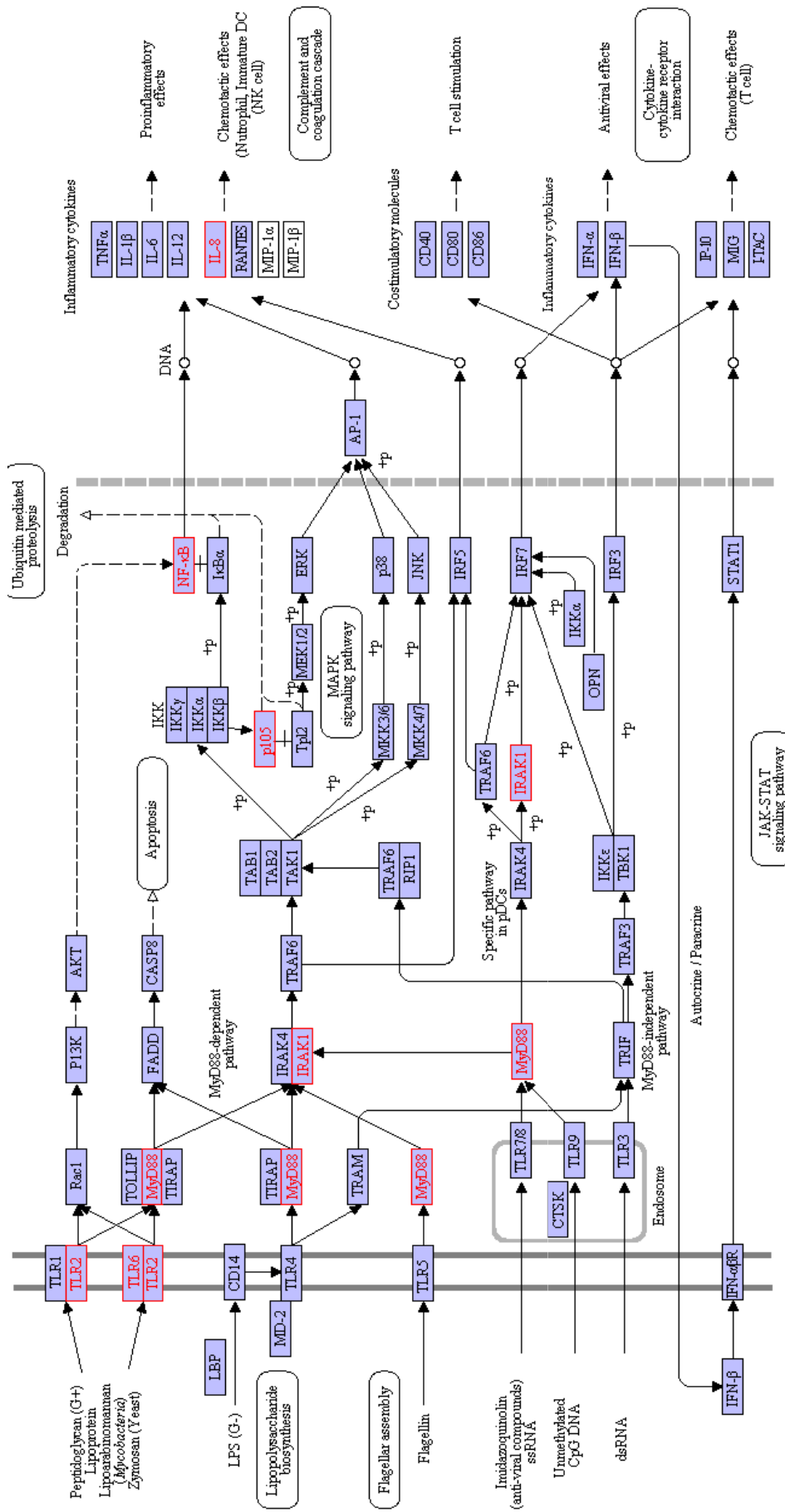
## **Supplementary Note**

### **(Quesada *et al.*, Exome-Sequencing Identifies Recurrent Mutations of the Splicing Factor SF3B1 in Chronic Lymphocytic Leukemia)**

The clinical and biological characteristics of the 105 patients selected for exome-sequencing are shown in **Supplementary Table 1**. Among these patients, which form a population-based cohort, 45 had *IGHV*-unmutated genes, and 60 *IGHV*-mutated genes (<98% identity). The tumor samples used for exome sequencing were obtained before administration of any treatment. The four patients previously examined by WGS and exome sequencing were not included in the present study. All patients gave informed consent for their participation in the study following the International Cancer Genome Consortium (ICGC) guidelines. To determine the clinical impact of *SF3B1* mutations, we expanded the study to 174 additional patients with CLL and 156 with non-Hodgkin's lymphomas. The clinical and biological characteristics of these patients are summarized in **Supplementary Table 14**. The patients with non-Hodgkin's lymphomas were selected based on the availability of frozen tissue with a confirmed tumor component. The diagnosis of these cases were 44 follicular lymphomas, 47 mantle cell lymphomas, 7 splenic marginal zone lymphomas, 51 diffuse large B-cell lymphomas and 7 peripheral T-cell lymphomas. The patients for this mutational screening and clinical validation agreed to an Institutional Review Board-approved informed consent for genetic studies.

The tumor samples used for exome sequencing were obtained from fresh or cryopreserved mononuclear cells. To purify the CLL fraction, samples were incubated with a cocktail of magnetically-labelled antibodies directed against T cells, NK cells, monocytes and granulocytes (CD2, CD3, CD11b, CD14, CD15 and CD56), adjusted to the percentage of each contaminating population (AutoMACS, Miltenyi Biotec). The degree of contamination by non-CLL cells in the CLL fraction was assessed by immunophenotype and flow cytometry. Whole blood was sedimented by 2% dextran and the leukocyte fraction was obtained. DNA was extracted from purified samples by using a Qiagen kit, and the quality of purified DNA was assessed by SYBR-green staining on agarose gels and

quantified using Nanodrop ND-100 spectrophotometer. The tumor DNA samples for exome sequencing contained  $\geq 95\%$  neoplastic cells and the contamination by neoplastic cells in normal DNA was  $< 2\%$ . The samples for the CLL validation cohort contained  $> 30\%$  neoplastic cells



**Supplementary Figure 1. Mutations in components of Toll-like receptor signaling pathways. The KEGG (<http://www.genome.jp/kegg/>) pathway including Toll-like receptor signaling is depicted. Somatic mutated genes in CLL are highlighted in red.**

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Haa_SF3B1 : KRKRWD OTADOTPGA-----TPKKLSWDQAEPTGHTPSLRWDETPGRAKSGSETGATP---GSKLMDPHESHTPAGAAATPGRGDTPGHGATSSARKRWDTPKTE-----R : 301
Dme_SF3B1 : KRKRWL QTVSDSFI PAKMATPSSAATPTWEDK-----TPGDHRWDETPG-KHKGSEI PGMAT-GLGTRLMDAIFAHAVT-----PGHETPGH---EKSSARRKWDTPKTE-----R : 305
Cel_1_SF3B1 : KRKRWLAEAPSTDAASNDTASATPSQGSAPRKRILG-----FSKISADAF-----RAARWDEIFAHSTG-----AADATP SVYDKWSTTPAQAQTPRRNRWDETPKEN-----L : 285
Ani_1_SF3B1 : KLLAEKQARGENGVOEHEATLKLDDKENAEAG-----STVSVAIGRKRKQWVVAHDETP-----AAPTSDDAKAKKSWDQAPAG----- : 256
Osa_1_SF3B1 : KRKRWLQS QEDDEGDAAGAKKAKTA-----SSSSSHWDAAP-----DAATP-----GIGRWDAIFGRAGG-----ATP SLKRRWDETPFGRWADAD : 370

Haa_SF3B1 : DTPCHGSGVAETPRTRDK-----GGDSIGETPTGAKRKRWTEPASOMGG-----STPVLTPG-KTFLICTPAMNATTPGHIMSMIPBGLCAWRWER : 390
Dme_SF3B1 : ETPGH-SGVAETPKPDRTPGSGGAESISIESTGPKRRSRWTEPENA TPA TPNV SAMTNPMTPTSMTPHVP GHATPMLTPFGGATP LCKAMAMAE SAGALAMIPBGLCAWRWK : 424
Cel_1_SF3B1 : NDGSMITPQGMETPARG-----GSDDVKIEDTISAKRKRSRWLIPTSQTFN-----VAATPLHSGLQTF SFTPSHP SQPTIGAMT PGGTICTAAMGKATAP-HMTFMIPBGLCAWRWK : 397
Ani_1_SF3B1 : -----CGEAPKRRSRMTQAP-----AI AATVINGGLATPWHPSQVGAHAEITSG-----T : 304
Osa_1_SF3B1 : GTPAPSVADSS-----TPTPQKQSRWTEIFAGVGS-----TAPRATDAVPAGVAPGHTPDAADLAPSGQIARGHMLPBGYCLLRWER : 454

Haa_SF3B1 : EIDERNPLSDEIDAMFP-EGKVMLEPPAGYVPIRPAKLIATPILFLGGMGFMHMDERT------MKSVNDQ-SG-NLEFLKPIEIOVDFLLVDVIES-TLSPEOERMI : 497
Dme_SF3B1 : EIDERNPLSDEIDQIFP-PGKLEPPAGYVPIRPAKLIATPILFLGGMGFMHMDERT------AKFMNQ-KQNL-EMKPEAQAQDFLLVDVIED-SLSPEELERMI : 533
Cel_1_SF3B1 : EIDERNPLSDEIDSLP-PGKVMLEPPAGYVPIRPAKLIATPILFLGGMGFMHMDERT------KNAEFLPKPFGKQVDFLLVDVIED-SLSPEELERMI : 515
Ani_1_SF3B1 : DJGRNPLSDEIDAMLPSEGVKLEPPAGYVPIRPAKLIATPILFLGGMGFMHMDERT------KOLPTELOFRPPEMAMFGALMDTGFDS-TMWSPEELERMI : 420
Osa_1_SF3B1 : EIDERNPLSDEIDTMLPQVGVKLEPPAGYVPIRPAKLIATPILFLGGMGFMHMDERT------QQFDVPEKLPFCGLQMKPEYVDFGFLNBEGESEKLSPEELERMI : 563

Haa_SF3B1 : MKLLTKNGSPARKALROITDKAEFGAGPLFNGILPLLASPELEDOERHLVKVDDRILYKLDLVRP VHKILVVEP LLEDEDIYARVEGERIISNLAKAAGLATMISTWRPDI : 617
Dme_SF3B1 : MKLLTKNGSPARKSLROITDKAEFGAGPLFNGILPLLASPELEDOERHLVKVDDRILYKLDLVRP VHKILVVEP LLEDEDIYARVEGERIISNLAKAAGLATMISTWRPDI : 653
Cel_1_SF3B1 : MEHLTKNGSPARKALROITDKAEFGAGPLFNGILPLLASPELEDOERHLVKVDDRILYKLDLVRP VHKILVVEP LLEDEDIYARVEGERIISNLAKAAGLATMISTWRPDI : 635
Ani_1_SF3B1 : MRLLTKNGSPARKALROITDKAEFGAGPLFNGILPLLASPELEDOERHLVKVDDRILYKLDLVRP VHKILVVEP LLEDEDIYARVEGERIISNLAKAAGLATMISTWRPDI : 540
Osa_1_SF3B1 : LKLEFRKNGSPARKALROITDKAEFGAGPLFNGILPLLASPELEDOERHLVKVDDRILYKLDLVRP VHKILVVEP LLEDEDIYARVEGERIISNLAKAAGLATMISTWRPDI : 683

Haa_SF3B1 : DNWDEAVNVTARAFVVA SNLGIFSLPFLAVCKSKSOWARHC KLVQOALMCGCALPHSRVSEIIEHGVDEQKVRTSALALALABAIPYGIESFDSVLKPLMGLIQ : 737
Dme_SF3B1 : DNWDEAVNVTARAFVVA SNLGIFSLPFLAVCKSKSOWARHC KLVQOALMCGCALPHSRVSEIIEHGVDEQKVRTSALALALABAIPYGIESFDSVLKPLMGLIQ : 773
Cel_1_SF3B1 : MEHLTKNGSPARKALROITDKAEFGAGPLFNGILPLLASPELEDOERHLVKVDDRILYKLDLVRP VHKILVVEP LLEDEDIYARVEGERIISNLAKAAGLATMISTWRPDI : 755
Ani_1_SF3B1 : DNWDEAVNVTARAFVVA SNLGIFSLPFLAVCKSKSOWARHC KLVQOALMCGCALPHSRVSEIIEHGVDEQKVRTSALALALABAIPYGIESFDSVLKPLMGLIQ : 660
Osa_1_SF3B1 : DNWDEAVNVTARAFVVA SNLGIFSLPFLAVCKSKSOWARHC KLVQOALMCGCALPHSRVSEIIEHGVDEQKVRTSALALALABAIPYGIESFDSVLKPLMGLIQ : 803

Haa_SF3B1 : HRGSLAAFLKAGLIPLMDAEVANYTIEVALILREFCSPDEEMKVLKVIQCCCTGVEANVYKTEILPEFFHFVORHMAIDRRNYQIVDTTVEIPANKVGAEEISRIVDIL : 857
Dme_SF3B1 : HRGSLAAFLKAGLIPLMDAEVANYTIEVALILREFCSPDEEMKVLKVIQCCCTGVEANVYKTEILPEFFHFVORHMAIDRRNYQIVDTTVEIPANKVGAEEISRIVDIL : 893
Cel_1_SF3B1 : HRGSLAAFLKAGLIPLMDAEVANYTIEVALILREFCSPDEEMKVLKVIQCCCTGVEANVYKTEILPEFFHFVORHMAIDRRNYQIVDTTVEIPANKVGAEEISRIVDIL : 875
Ani_1_SF3B1 : HRGSLAAFLKAGLIPLMDAEVANYTIEVALILREFCSPDEEMKVLKVIQCCCTGVEANVYKTEILPEFFHFVORHMAIDRRNYQIVDTTVEIPANKVGAEEISRIVDIL : 780
Osa_1_SF3B1 : HRGSLAAFLKAGLIPLMDAEVANYTIEVALILREFCSPDEEMKVLKVIQCCCTGVEANVYKTEILPEFFHFVORHMAIDRRNYQIVDTTVEIPANKVGAEEISRIVDIL : 923

Haa_SF3B1 : KDPAEORRQVMEHEHEDMGNIGADHDHKEBOLLELCIYAFORQITDS-MLGFTVTVALCKRKPFPPOICGIVMLINKSAVROAADLISRVAVMVTCCEKLMGHICV : 976
Dme_SF3B1 : KDNPEORRQVMEHEHEDMGNIGADHDHKEBOLLELCIYAFORQITDS-MLGFTVTVALCKRKPFPPOICGIVMLINKSAVROAADLISRVAVMVTCCEKLMGHICV : 1012
Cel_1_SF3B1 : KDNPEORRQVMEHEHEDMGNIGADHDHKEBOLLELCIYAFORQITDS-MLGFTVTVALCKRKPFPPOICGIVMLINKSAVROAADLISRVAVMVTCCEKLMGHICV : 994
Ani_1_SF3B1 : KDSSEPRKRVMEHEHEDMGNIGADHDHKEBOLLELCIYAFORQITDS-MLGFTVTVALCKRKPFPPOICGIVMLINKSAVROAADLISRVAVMVTCCEKLMGHICV : 899
Osa_1_SF3B1 : KDSSEPRKRVMEHEHEDMGNIGADHDHKEBOLLELCIYAFORQITDS-MLGFTVTVALCKRKPFPPOICGIVMLINKSAVROAADLISRVAVMVTCCEKLMGHICV : 1043

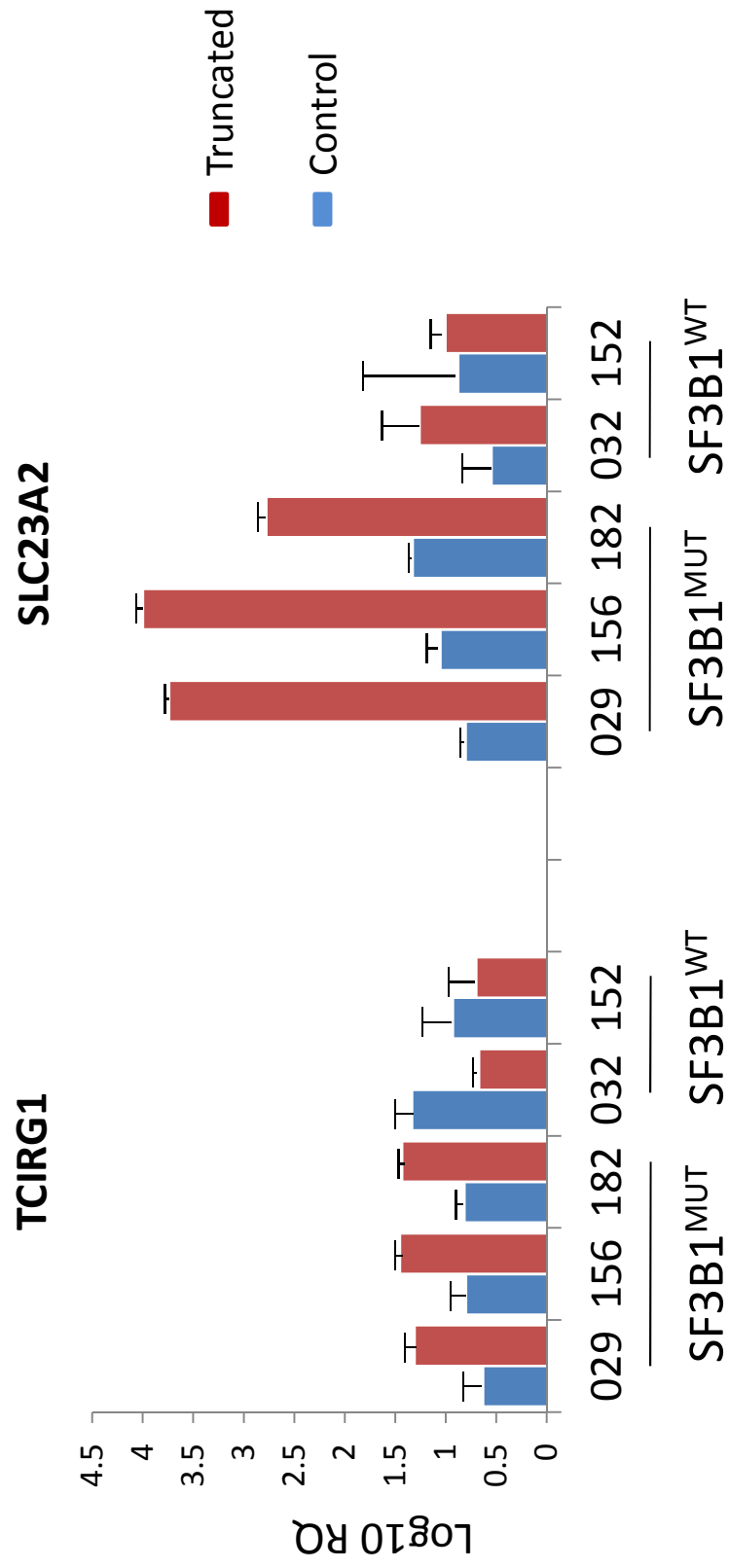
Haa_SF3B1 : VLVEPLGEEYPEVLGSLGALKALVAVIGMHTMPPIDLLPRLTPTIKNRHEKVOBNCIDLVRGADRCAEVSAREWIRIGFELLEPKAKHKAIRRAVNTVFCILAKAIGPHDVLAT : 1096
Dme_SF3B1 : VLVEPLGEEYPEVLGSLGALKALVAVIGMHTMPPIDLLPRLTPTIKNRHEKVOBNCIDLVRGADRCAEVSAREWIRIGFELLEPKAKHKAIRRAVNTVFCILAKAIGPHDVLAT : 1132
Cel_1_SF3B1 : VLVEPLGEEYPEVLGSLGALKALVAVIGMHTMPPIDLLPRLTPTIKNRHEKVOBNCIDLVRGADRCAEVSAREWIRIGFELLEPKAKHKAIRRAVNTVFCILAKAIGPHDVLAT : 1114
Ani_1_SF3B1 : VLVEPLGEEYPEVLGSLGALKALVAVIGMHTMPPIDLLPRLTPTIKNRHEKVOBNCIDLVRGADRCAEVSAREWIRIGFELLEPKAKHKAIRRAVNTVFCILAKAIGPHDVLAT : 1019
Osa_1_SF3B1 : VLVEPLGEEYPEVLGSLGALKALVAVIGMHTMPPIDLLPRLTPTIKNRHEKVOBNCIDLVRGADRCAEVSAREWIRIGFELLEPKAKHKAIRRAVNTVFCILAKAIGPHDVLAT : 1163

Haa_SF3B1 : LLNNLVAQERQNRVCTVAIVAEICSPFTVLPALMNEVRVPEHNVONGVLALESFPEYIGEMGKDYIYAVTPLEDALMDRDVHRQVFAVAICMSLGVVYFCGCBESHLNLYYW : 1216
Dme_SF3B1 : LLNNLVAQERQNRVCTVAIVAEICSPFTVLPALMNEVRVPEHNVONGVLALESFPEYIGEMGKDYIYAVTPLEDALMDRDVHRQVFAVAICMSLGVVYFCGCBESHLNLYYW : 1252
Cel_1_SF3B1 : LLNNLVAQERQNRVCTVAIVAEICSPFTVLPALMNEVRVPEHNVONGVLALESFPEYIGEMGKDYIYAVTPLEDALMDRDVHRQVFAVAICMSLGVVYFCGCBESHLNLYYW : 1234
Ani_1_SF3B1 : LLNNLVAQERQNRVCTVAIVAEICSPFTVLPALMNEVRVPEHNVONGVLALESFPEYIGEMGKDYIYAVTPLEDALMDRDVHRQVFAVAICMSLGVVYFCGCBESHLNLYYW : 1139
Osa_1_SF3B1 : LLNNLVAQERQNRVCTVAIVAEICSPFTVLPALMNEVRVPEHNVONGVLALESFPEYIGEMGKDYIYAVTPLEDALMDRDVHRQVFAVAICMSLGVVYFCGCBESHLNLYYW : 1282

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■ U2AF65 binding  
■ p14 binding  
■ HEAT

Supplementary Figure 2. Multiple sequence alignment of SF3B1 from representative eukaryotic species. Conserved residues are shaded. Mutated residues are highlighted in red. Hsa, *Homo sapiens*; Dme, *Drosophila melanogaster*; Cel, *Caenorhabditis elegans*; Ani, *Aspergillus nidulans*; Osa, *Oryza sativa*.



**Supplementary Figure 3. Novel splicing forms in *TCIRG1* and *SLC23A2* associated with mutations in *SF3B1*.** Comparison of three *SF3B1*-mutated cases with two *SF3B1*-unmutated cases by quantitative RT-PCR. Error bars represent standard deviations.

**Supplementary Table 1.** Clinical features of the patients

Variable	Category	
Sex	Male /Female	68 / 37
Age, median (range)		62 (34-93) years
Clinical status at sampling	Stable disease	51/105 (49%)
	Progression	54/105 (51%)
Binet stage	A	97 (92%)
	B	6 (6%)
	C	2 (2%)
Rai stage	0	65 (62%)
	I-II	37 (35%)
Binet stage (at sampling time)*	III-IV	3 (3%)
	A	58 (57%)
Rai stage (at sampling time)*	B	29 (28%)
	C	15 (15%)
	0	40 (39%)
Lymphocytes (x10 <sup>9</sup> /L), median (range)	I-II	44 (43%)
	III-IV	18 (18%)
Hemoglobin (g/L), median (range)		13 (2.6-80)
Platelets (x10 <sup>9</sup> /L), median (range)		140 (93-175)
LDH	>UNL	204 (21-470)
β <sub>2</sub> -microglobulin	>UNL	8/100 (8%)
Lymphocyte doubling time	< 1 year	25/92 (27%)
CD38	High	15/84 (18%)
ZAP-70	High	26/100 (26%)
IGHV	Unmutated	28/97 (29%)
	del(13)(q14.3)	45/105 (43%)
	del(11)(q22.3)	50/104 (48%)
	12	14/104 (14%)
	del(17)(p13.1)	10/104 (10%)
Genetic abnormality (at sampling time)		1/104 (1%)
10-year time PFS (95% CI)	Binet stage A	46% (34-58)
10-year OS (95% CI)	All	82% (73-91)
Follow-up, median (range)	All	6.6 (0.6-23) years

Clinical status at sampling: Stable disease (no criteria for therapy), progression (requiring therapy) (sampling always before starting treatment); CD38 high: ≥ 30% positive CLL cells; ZAP-70 high: ≥ 20% positive CLL cells; IGHV unmutated: ≥ 98% homology with germline; PFS: progression-free survival; OS: overall survival. \*Stage information was not available for three patients at sampling time.

**Supplementary Table 2.** Biological characteristics of the tumor samples

Case	IGHV mutational status	NOTCH1	SF3B1	ZAP-70	CD38
005	Unmutated	Unmutated	Unmutated	64	20
006	Unmutated	Unmutated	N626Y	77	100
007	Mutated	Unmutated	Unmutated	16	2
008	Unmutated	Unmutated	Unmutated	42	85
009	Mutated	Unmutated	K700E	5	10
013	Unmutated	Unmutated	Unmutated	57	18
016	Unmutated	Unmutated	Unmutated	67	0
017	Unmutated	Unmutated	Unmutated	77	45
018	Mutated	Unmutated	Unmutated	13	0
019	Mutated	P2515Rfs*4	V701F	10	88
020	Unmutated	Unmutated	Unmutated	44	44
022	Unmutated	Unmutated	Unmutated	42	32
023	Unmutated	Unmutated	Unmutated	18	90
027	Unmutated	Unmutated	Unmutated	1	0
029	Unmutated	Unmutated	K700E	13	18
030	Unmutated	Unmutated	Unmutated	18	79
032	Mutated	Unmutated	Unmutated	1	97
033	Mutated	Unmutated	Unmutated		25
038	Unmutated	Unmutated	Unmutated	30	80
039	Mutated	Unmutated	Unmutated	0,4	2,5
040	Mutated	Unmutated	Unmutated	2	1
041	Mutated	Unmutated	Unmutated	36	11
042	Unmutated	Unmutated	Unmutated	14	13
043	Mutated	Unmutated	Unmutated	12	10
044	Unmutated	Unmutated	Unmutated	26	26
045	Mutated	Unmutated	Unmutated	9	91
048	Unmutated	P2515Rfs*4	Unmutated	65	98
049	Unmutated	Unmutated	Unmutated	63	1
051	Mutated	Unmutated	Unmutated	6	8
052	Unmutated	Unmutated	Unmutated	3	2
053	Unmutated	Unmutated	T663I	21	18
054	Unmutated	Unmutated	Unmutated	25	98
063	Unmutated	Unmutated	Unmutated	7	87
064	Mutated	Unmutated	Unmutated	0,9	16
082	Unmutated	Unmutated	Unmutated	2	70
083	Unmutated	Unmutated	D894G	60	97
090	Mutated	Unmutated	Unmutated	3	0
091	Mutated	Unmutated	Unmutated	4	14
100	Unmutated	Unmutated	Unmutated	39	48
110	Mutated	Unmutated	Unmutated	6	13
117	Mutated	Unmutated	Unmutated	7	8
124	Mutated	Unmutated	Unmutated	1	2
136	Mutated	Unmutated	Unmutated	1	5
141	Unmutated	Unmutated	Unmutated	24	87
144	Mutated	Unmutated	Unmutated	51,5	0

145	Unmutated	Unmutated	Unmutated	8	99
146	Mutated	Unmutated	Unmutated	7	14
148	Unmutated	Unmutated	Unmutated	48	90
152	Mutated	Unmutated	Unmutated	14	7
155	Unmutated	Unmutated	Unmutated	0	0
156	Mutated	P2515Rfs*4	K700E	0	54
157	Unmutated	Unmutated	Unmutated	0	13
159	Mutated	Unmutated	Unmutated	1	1,5
165	Mutated	Unmutated	Unmutated	1	10
166	Unmutated	Unmutated	Unmutated	84	90
168	Mutated	Unmutated	Unmutated	13	2
170	Mutated	Unmutated	Unmutated	1,5	2
171	Mutated	Unmutated	Unmutated	4	5
172	Mutated	Unmutated	Unmutated	3	10
173	Mutated	Unmutated	Unmutated	3	0
174	Mutated	Unmutated	Unmutated	4	2
175	Mutated	Unmutated	Unmutated	1,5	3
178	Mutated	Unmutated	Unmutated		94
181	Mutated	Unmutated	Unmutated	4	2
182	Unmutated	Unmutated	N626Y	18	21
184	Unmutated	P2515Rfs*4	Unmutated	70	30
185	Mutated	Unmutated	Unmutated	1	0
186	Unmutated	Unmutated	Unmutated	26	10
188	Unmutated	Unmutated	Unmutated	14	1
189	Mutated	Unmutated	Unmutated	17	5
191	Mutated	Unmutated	Unmutated	0,3	0
192	Mutated	Unmutated	Unmutated	4	0
193	Mutated	Unmutated	Unmutated	14	4
194	Mutated	Unmutated	Unmutated	1	15
195	Unmutated	Unmutated	Unmutated	70	3
197	Mutated	Unmutated	G742D	2	16
264	Mutated	Unmutated	Unmutated	1	16
266	Mutated	Unmutated	Unmutated	0	2
267	Mutated	Unmutated	Unmutated	3	5
270	Unmutated	Unmutated	Unmutated	9	8
272	Mutated	Unmutated	Unmutated	12	4
273	Mutated	Unmutated	Unmutated	1	1
274	Mutated	Unmutated	Unmutated	8	0
275	Unmutated	Unmutated	Unmutated	70	10
276	Mutated	Unmutated	Unmutated	14	0
278	Unmutated	Unmutated	Unmutated	11	1
279	Unmutated	Unmutated	Unmutated	19	20
280	Mutated	Unmutated	Unmutated	2	8
282	Unmutated	Unmutated	Unmutated	50	2
290	Unmutated	Unmutated	Unmutated	25	98
319	Mutated	Unmutated	Unmutated		
321	Unmutated	P2515Rfs*4	Unmutated	0	29
322	Mutated	Unmutated	Unmutated		
323	Mutated	Unmutated	Unmutated	0	0
324	Mutated		Unmutated		



325	Unmutated	Unmutated	Unmutated		
326	Unmutated	Unmutated	Unmutated		0
328	Mutated	Unmutated	Unmutated		
375	Mutated	Unmutated	Unmutated	0,9	0,35
618	Mutated	Unmutated	Unmutated	17	0
642	Mutated	Unmutated	Unmutated	1	2
680	Mutated	Unmutated	Unmutated	29	26
758	Mutated	Unmutated	K700E	14	28
761	Unmutated	Unmutated	Unmutated	8	47
785	Mutated	Unmutated	Unmutated	14	3

**Supplementary Table 3.** Statistics for whole-exome sequencing

Case	Sample	Number of reads mapped	Depth	Coverage	Cov. $\geq 10$
005	Normal	53717781	57	97.40%	88.5%
	Tumor	59238351	62	97.60%	89.2%
006	Normal	59756858	61	97.20%	88.7%
	Tumor	56627266	57	97.50%	89.2%
007	Normal	54734688	59	97.50%	87.9%
	Tumor	56808871	59	97.60%	88.8%
008	Normal	55941286	59	96.60%	86.9%
	Tumor	55259258	61	97.60%	89.0%
009	Normal	60605942	62	97.80%	89.3%
	Tumor	58515451	59	97.60%	89.0%
013	Normal	61943019	64	97.20%	89.0%
	Tumor	63144498	67	97.10%	88.3%
016	Normal	100132780	131	85.30%	79.3%
	Tumor	96631049	125	85.20%	79.4%
017	Normal	57200757	60	97.60%	89.4%
	Tumor	48334046	57	97.50%	88.7%
018	Normal	55310757	58	97.80%	88.9%
	Tumor	62114147	64	97.50%	88.5%
019	Normal	57997219	63	97.40%	87.9%
	Tumor	58655271	61	97.70%	89.4%
020	Normal	60747151	64	97.60%	89.6%
	Tumor	59051980	61	97.60%	89.7%
022	Normal	58181093	61	97.40%	89.2%
	Tumor	58761948	61	97.30%	88.8%
023	Normal	60290894	62	97.70%	89.6%
	Tumor	53940646	59	97.10%	87.8%
027	Normal	60857180	62	97.70%	90.1%
	Tumor	62882050	63	97.20%	87.8%
029	Normal	59032114	60	97.70%	89.5%
	Tumor	63058990	64	97.30%	89.1%
030	Normal	60322038	60	97.60%	88.8%
	Tumor	63698075	65	97.30%	88.1%
032	Normal	67107448	66	97.40%	88.7%
	Tumor	60843934	63	97.70%	89.0%
033	Normal	59752194	60	97.50%	88.3%
	Tumor	40224131	41	95.30%	82.4%
038	Normal	64263020	65	97.60%	89.1%
	Tumor	64058844	65	97.50%	88.9%
039	Normal	52591525	53	97.40%	88.0%
	Tumor	66444563	66	97.10%	87.1%
040	Normal	53413657	54	97.40%	87.9%
	Tumor	57471264	58	97.40%	88.8%
041	Normal	61880545	64	97.60%	89.4%
	Tumor	59912603	61	97.40%	88.5%
042	Normal	59125142	58	97.10%	86.7%
	Tumor	57857463	59	97.40%	88.0%

043	Normal	40833305	48	97.00%	86.5%
	Tumor	57639174	59	97.40%	88.1%
044	Normal	62362894	63	97.70%	89.3%
	Tumor	58962155	59	97.60%	88.8%
045	Normal	62843286	65	97.30%	89.5%
	Tumor	62599964	64	97.30%	89.0%
048	Normal	59775498	64	96.90%	86.4%
	Tumor	54564216	58	97.30%	87.8%
049	Normal	61163114	64	97.50%	89.3%
	Tumor	59511868	61	97.30%	88.8%
051	Normal	64713633	67	97.10%	87.9%
	Tumor	61218409	64	97.60%	89.3%
052	Normal	58002379	61	97.50%	88.6%
	Tumor	53489476	57	97.40%	87.9%
053	Normal	61732639	63	97.70%	90.1%
	Tumor	62763508	67	97.50%	88.8%
054	Normal	57003861	58	97.30%	88.4%
	Tumor	61827623	64	97.20%	88.7%
063	Normal	60381172	64	97.60%	89.6%
	Tumor	53128282	55	97.80%	89.4%
064	Normal	59743847	62	97.60%	89.5%
	Tumor	55685113	57	97.60%	88.5%
082	Normal	52268280	56	97.00%	87.4%
	Tumor	63595364	66	97.00%	87.6%
083	Normal	53232286	57	97.20%	88.1%
	Tumor	60339913	63	97.20%	88.5%
090	Normal	56830982	60	97.40%	89.0%
	Tumor	57647029	61	97.00%	88.1%
091	Normal	55143096	59	97.50%	89.9%
	Tumor	62483620	66	97.00%	87.6%
100	Normal	53006576	58	97.70%	89.5%
	Tumor	61816215	66	97.10%	87.7%
110	Normal	62336370	65	97.20%	89.1%
	Tumor	61862080	65	96.90%	87.7%
117	Normal	50722217	53	97.00%	87.2%
	Tumor	59237338	60	97.20%	88.0%
124	Normal	63588439	65	97.50%	89.2%
	Tumor	59057669	62	97.50%	89.1%
136	Normal	63828805	69	96.80%	87.7%
	Tumor	63753438	66	97.20%	88.4%
141	Normal	59931810	62	97.50%	88.8%
	Tumor	57202992	60	97.40%	88.0%
144	Normal	63616079	65	97.60%	88.9%
	Tumor	60153070	61	97.40%	88.1%
145	Normal	58570386	62	97.30%	88.6%
	Tumor	57642285	62	97.60%	89.1%
146	Normal	59552541	63	97.50%	89.0%
	Tumor	62139557	67	97.60%	89.5%
148	Normal	72715382	80	97.60%	89.9%
	Tumor	58166761	61	97.90%	90.0%

152	Normal	56213419	59	97.90%	90.1%
	Tumor	49302140	53	97.70%	89.6%
155	Normal	51727153	56	97.50%	89.0%
	Tumor	60802199	66	97.40%	89.1%
156	Normal	78114226	82	97.50%	89.3%
	Tumor	40919535	44	97.70%	88.0%
157	Normal	62939680	66	97.90%	90.70%
	Tumor	62263826	67	97.80%	90.90%
159	Normal	55080126	58	97.70%	89.40%
	Tumor	57245641	62	97.40%	88.10%
165	Normal	50610537	52	97.40%	88.40%
	Tumor	51913777	56	97.50%	89.40%
166	Normal	47943642	49	97.00%	86.70%
	Tumor	50297712	54	97.70%	88.20%
168	Normal	59888030	61	97.70%	89.00%
	Tumor	64947770	64	97.50%	89.80%
170	Normal	60657128	68	97.30%	87.90%
	Tumor	62590312	69	97.10%	87.20%
171	Normal	50958302	53	97.10%	87.10%
	Tumor	48620622	55	97.00%	86.90%
172	Normal	52512304	54	97.40%	88.00%
	Tumor	49481425	53	97.10%	87.80%
173	Normal	53456012	54	97.60%	88.40%
	Tumor	63007729	70	97.30%	88.00%
174	Normal	49000882	49	97.30%	88.20%
	Tumor	58804984	57	97.50%	88.80%
175	Normal	54233281	57	97.60%	88.80%
	Tumor	53139627	58	97.70%	88.90%
178	Normal	58716794	63	97.70%	89.60%
	Tumor	50485234	53	97.50%	88.20%
181	Normal	53840639	57	97.60%	88.60%
	Tumor	53790387	57	97.70%	89.00%
182	Normal	52272456	56	97.70%	89.80%
	Tumor	42695862	40	97.40%	85.50%
184	Normal	56842387	61	98.00%	90.90%
	Tumor	67812616	72	98.10%	90.90%
185	Normal	69469540	71	97.80%	90.20%
	Tumor	49186172	57	97.70%	90.00%
186	Normal	57466878	60	97.90%	90.20%
	Tumor	57666748	62	97.70%	90.30%
188	Normal	63758567	64	97.60%	89.50%
	Tumor	60959293	64	97.30%	88.90%
189	Normal	63146282	63	97.00%	88.40%
	Tumor	59302580	60	97.00%	87.80%
191	Normal	65762885	69	97.90%	90.40%
	Tumor	53500566	61	97.70%	90.20%
192	Normal	36260479	44	97.50%	88.40%
	Tumor	74879197	78	97.50%	90.40%
193	Normal	62844879	63	96.80%	87.60%
	Tumor	51953554	55	96.90%	87.70%

194	Normal	60762734	63	97.00%	88.40%
	Tumor	60679454	62	96.90%	88.30%
195	Normal	69064237	74	97.90%	90.60%
	Tumor	74020561	80	98.20%	92.90%
197	Normal	57500804	64	97.60%	90.30%
	Tumor	67337694	70	97.40%	90.40%
264	Normal	67688335	76	97.90%	91.00%
	Tumor	45032303	53	97.90%	89.90%
266	Normal	46682286	55	97.90%	90.40%
	Tumor	59185829	68	97.70%	90.30%
267	Normal	74254940	74	97.70%	90.10%
	Tumor	69609754	74	97.80%	90.90%
270	Normal	57103246	65	97.90%	90.50%
	Tumor	71804250	76	97.90%	90.90%
272	Normal	60643107	63	97.70%	90.40%
	Tumor	57024005	60	97.50%	89.30%
273	Normal	65944135	69	97.80%	90.50%
	Tumor	69152356	72	97.90%	90.70%
274	Normal	77822287	81	97.20%	89.10%
	Tumor	53762072	62	97.70%	89.90%
275	Normal	69022253	69	97.50%	90.50%
	Tumor	56194776	61	97.70%	90.10%
276	Normal	68465274	71	98.00%	90.80%
	Tumor	67477376	72	97.90%	90.60%
278	Normal	69027081	71	98.10%	90.70%
	Tumor	65688812	70	97.90%	90.80%
279	Normal	69759299	76	98.10%	91.70%
	Tumor	72194501	75	97.60%	90.50%
280	Normal	62826127	63	96.80%	87.70%
	Tumor	66321483	67	97.20%	88.80%
282	Normal	49234680	50	97.30%	87.90%
	Tumor	56083825	57	97.20%	88.30%
290	Normal	61987314	64	97.30%	89.10%
	Tumor	59423536	61	97.20%	89.20%
319	Normal	52558321	53	97.90%	89.40%
	Tumor	37574677	39	97.70%	86.70%
321	Normal	46117028	49	97.40%	88.80%
	Tumor	54668728	55	97.40%	88.90%
322	Normal	45039378	48	97.90%	88.60%
	Tumor	49538770	52	97.70%	88.90%
323	Normal	62289392	64	97.60%	90.30%
	Tumor	60899478	64	97.70%	90.10%
324	Normal	59678081	60	97.60%	89.40%
	Tumor	55187765	58	97.60%	89.70%
325	Normal	62147834	64	97.20%	88.80%
	Tumor	57957790	63	97.30%	89.10%
326	Normal	70135169	69	97.80%	90.40%
	Tumor	39917823	45	96.70%	85.90%
328	Normal	60612086	65	97.90%	90.80%
	Tumor	50151522	61	97.70%	90.10%

375	Normal	74615242	78	98.00%	91.20%
	Tumor	58887793	61	98.00%	90.30%
618	Normal	54873020	58	97.80%	89.90%
	Tumor	61769937	66	97.60%	89.70%
642	Normal	56110386	59	97.50%	89.60%
	Tumor	63124269	65	97.40%	90.10%
680	Normal	59002206	63	97.40%	89.40%
	Tumor	57915382	61	97.70%	89.60%
758	Normal	55111696	60	97.40%	88.50%
	Tumor	55438717	58	97.70%	88.70%
761	Normal	58047340	62	97.60%	89.10%
	Tumor	49050366	52	97.60%	88.40%
785	Normal	55016679	61	97.50%	88.90%
	Tumor	56350701	57	97.60%	88.90%

**Supplementary Table 5.** Somatic mutations in CLL with predicted functional consequences

Case	Symbol	Mutation Type	Effect	Chr	Position	Ref	Obs
144	A2BP1	non_synonymous	E194D	16	7645604	G	S
375	A2ML1	non_synonymous	N1402D	12	9021782	A	R
043	AAMP	non_synonymous	C283S	2	219130588	C	S
043	AAMP	non_synonymous	D282A	2	219130591	T	K
159	ABCA12	non_synonymous	P376T	2	215891598	G	K
279	ABCA13	non_synonymous	A1262S	7	48313047	G	K
157	ABCA4	non_synonymous	P1342L	1	94497437	G	R
185	ABCA4	non_synonymous	S2213F	1	94463508	G	R
029	ABCB5	non_synonymous	A877T	7	20766666	G	R
181	ABCC11	non_synonymous	S294Y	16	48250095	G	K
019	ABCD1	non_synonymous	S606P	X	153008476	T	Y
157	ABCD2	non_synonymous	E374G	12	40001516	T	Y
159	ABCE1	non_synonymous	E307V	4	146038564	A	W
013	ABHD12	non_synonymous	G392S	20	25275650	C	Y
175	ABHD13	non_synonymous	S221N	13	108882228	G	R
321	ABI3BP	non_synonymous	R1065H	3	100535588	C	Y
165	ABR	non_synonymous	V510I	17	959308	C	Y
090	AC005921.3	frameshift	D386fs	17	48827881	*	+A
172	AC008026.2	non_synonymous	D47G	17	60460324	A	R
680	AC008749.3	non_synonymous	T277S	19	56284511	C	S
278	AC010201.1	non_synonymous	R14I	12	89893910	G	K
194	AC010974.2	non_synonymous	K183R	2	133721324	T	Y
019	AC011467.2	non_synonymous	R103W	19	22785450	C	Y
680	AC012555.1	non_synonymous	R249C	12	104255962	G	R
053	AC013486.2	splicing-site	-	15	74363379	G	M
006	AC022415.3	non_synonymous	T185N	19	12155803	G	K
270	AC023886.1	non_synonymous	H129Y	4	113506879	G	R
022	AC025016.1	non_synonymous	D130Y	11	5989019	C	M
172	AC069029.1	non_synonymous	V95M	15	99512742	C	Y
680	AC084121.1	non_synonymous	T58S	8	7627164	A	W
680	AC091435.2	frameshift	L228fs	5	38820752	*	-AAAGA
267	AC092070.5	non_synonymous	T118K	19	53786091	C	M
172	AC093331.1	non_synonymous	A69S	8	86556495	C	M
182	AC093331.1	non_synonymous	N159K	8	86556223	G	S
043	AC093844.4	non_synonymous	V137I	4	184243171	C	Y
172	AC099489.1	non_synonymous	D279G	16	11544661	T	Y
680	AC104758.5	non_synonymous	L82P	15	78233849	A	A
048	AC104819.1	non_synonymous	V40I	4	152200977	G	R
182	AC110754.1	non_synonymous	Q941R	2	11750969	A	R
005	AC111152.1	non_synonymous	Q128*	15	30337208	C	Y
319	AC126603.1	non_synonymous	L66H	15	20468102	A	W
322	AC128683.1	non_synonymous	D997N	3	130292811	G	R
020	AC131280.6	non_synonymous	M242I	15	20776661	G	K
053	AC135050.1	non_synonymous	L175Q	16	31072905	A	C
152	AC140658.4	non_synonymous	R487W	16	33716978	G	R
191	AC215219.4	non_synonymous	V146M	12	87908	G	R

027	ACACA	non_synonymous	G355E	17	35627697	C	Y
117	ACER1	non_synonymous	Y75C	19	6312286	T	Y
054	ACPT	non_synonymous	D110G	19	51294938	A	R
053	ADA	splicing-site	-	20	43264866	T	M
618	ADAM18	non_synonymous	P538T	8	39535036	C	A
013	ADAM2	non_synonymous	E181D	8	39666956	T	W
039	ADAM2	non_synonymous	L650V	8	39606897	G	S
016	ADAM29	non_synonymous	T746M	4	175898913	C	Y
013	ADAMTS13	non_synonymous	W669R	9	136310020	T	W
022	ADAMTS18	non_synonymous	R664C	16	77359805	G	R
033	ADAMTS18	non_synonymous	K528N	16	77387660	T	K
018	ADAMTS20	non_synonymous	L1001R	12	43826201	A	M
278	ADAMTS4	non_synonymous	D320Y	1	161166093	C	M
642	ADCY10	non_synonymous	V676I	1	167825548	C	Y
758	ADRBK1	non_synonymous	M229V	11	67048967	A	R
144	ADRBK2	non_synonymous	S168C	22	26063766	A	W
148	AFAP1	non_synonymous	A681V	4	7776486	G	R
279	AGAP6	non_synonymous	K295N	10	51768770	A	W
090	AGBL4	non_synonymous	M15V	1	50317182	T	Y
272	AHI1	non_synonymous	T1034A	6	135715923	T	Y
039	AHNAK	non_synonymous	N1026T	11	62298812	T	K
184	AK5	non_synonymous	R257H	1	77806132	G	R
324	AKAP12	non_synonymous	E1311A	6	151673458	A	M
192	AKAP13	non_synonymous	K809E	15	86123724	A	R
110	AKAP6	non_synonymous	T2288R	14	33293882	C	S
189	AKAP6	non_synonymous	R943*	14	33147613	C	Y
758	AKR1C4	non_synonymous	R7C	10	5238849	C	Y
184	AKT3	non_synonymous	K172Q	1	243800960	T	K
032	AL096711.2	non_synonymous	A848T	6	127796629	C	Y
325	AL353997.11	splicing-site	-	17	18332235	G	R
181	AL929601.2	non_synonymous	F47C	14	20085538	T	K
018	ALDH1L2	non_synonymous	M600I	12	105440551	C	Y
279	ALK	non_synonymous	V811M	2	29456487	C	Y
173	ALS2CL	non_synonymous	S650N	3	46718211	C	Y
270	ALS2CL	non_synonymous	A938E	3	46713130	G	K
171	ALS2CR11	non_synonymous	G540S	2	202400632	C	Y
168	ALX1	non_synonymous	Q198H	12	85680693	A	W
267	AMDHD2	non_synonymous	K120E	16	2571122	A	R
290	AMZ2	non_synonymous	P338L	17	66253040	C	Y
642	ANKAR	non_synonymous	V1111L	2	190597863	G	S
276	ANKRD17	non_synonymous	L677P	4	74008412	A	R
090	ANKRD40	non_synonymous	R177W	17	48777009	G	R
375	ANKRD61	non_synonymous	F399L	7	6075957	C	S
054	ANTXR1	non_synonymous	K451N	2	69409792	G	K
146	AOC2	non_synonymous	G463S	17	40998030	G	R
159	AP001011.3	non_synonymous	D184G	18	2674057	A	R
159	AP002478.3	non_synonymous	S50P	18	3596987	T	Y
275	AP003122.1	non_synonymous	T33M	11	89487037	G	R
324	AP003122.2	non_synonymous	N131H	11	89499960	T	K
194	AP004607.4	non_synonymous	G255V	11	89719141	C	M



145	AP2A2	non_synonymous	V382M	11	988564	G	R
006	APH1B	non_synonymous	T27I	15	63569902	C	Y
375	APOM	non_synonymous	H152Y	6	31625413	C	Y
043	ARG1	non_synonymous	F15L	6	131894467	C	M
159	ARHGAP20	non_synonymous	Q892K	11	110450996	G	K
013	ARHGAP28	non_synonymous	T715I	18	6898548	C	Y
110	ARHGAP28	non_synonymous	A71T	18	6824849	G	R
193	ARHGEF17	splicing-site	-	11	73076433	A	M
124	ARID1A	non_synonymous	P408L	1	27056227	C	Y
178	ARID1A	non_synonymous	R1276*	1	27099947	C	Y
282	ARNT2	non_synonymous	H543R	15	80872766	A	R
039	ASAP1	splicing-site	-	8	131249242	A	W
195	ASTN1	non_synonymous	P1108L	1	176852058	G	R
030	ASXL1	non_synonymous	E518*	20	31021553	G	K
145	ASXL1	frameshift	K686fs	20	31022572	*	-GT
182	ASXL1	non_synonymous	K838*	20	31023027	A	W
197	ASXL3	non_synonymous	N1746T	18	31325049	A	M
155	ATBF1	non_synonymous	A1099V	16	72923782	G	R
006	ATM	non_synonymous	L2033V	11	108186739	C	G
020	ATM	splicing-site	-	11	108141874	G	R
048	ATM	splicing-site	-	11	108165652	A	W
145	ATM	non_synonymous	A2626V	11	108203577	C	T
279	ATP10B	non_synonymous	T836I	5	160044890	G	R
038	ATP1A4	non_synonymous	F401L	1	160136473	T	W
040	ATP1B2	non_synonymous	R286C	17	7559196	C	Y
124	ATP2C2	non_synonymous	E403K	16	84473128	G	R
174	ATP8A2	non_synonymous	S260I	13	26116184	G	K
090	ATPGD1	non_synonymous	I578L	11	67191320	A	M
027	ATRX	non_synonymous	A224V	X	76940077	G	A
758	ATRX	non_synonymous	W222C	X	76940082	C	G
189	ATXN10	non_synonymous	T303K	22	46134624	C	M
324	B3GNT9	non_synonymous	N238K	16	67183675	A	W
091	BACH2	non_synonymous	G594R	6	90660045	C	Y
159	BARD1	non_synonymous	S162A	2	215646114	A	M
043	BAZ2B	non_synonymous	A1743T	2	160205255	C	Y
173	BCAT2	splicing-site	-	19	49299833	T	M
053	BCL11B	non_synonymous	T845M	14	99640639	G	A
141	BCOR	non_synonymous	Y657*	X	39932628	G	T
194	BDKRB1	non_synonymous	N114I	14	96730360	A	W
027	BFSP2	non_synonymous	Y210C	3	133167389	A	R
018	BIRC2	non_synonymous	W316R	11	102221625	T	Y
044	BIRC6	non_synonymous	L3687R	2	32740548	T	K
267	BLM	non_synonymous	H805Y	15	91312674	C	Y
322	BLZF1	non_synonymous	A296S	1	169351388	G	K
319	BMP10	non_synonymous	D403E	2	69092829	G	K
326	BNC1	non_synonymous	R611C	15	83932172	G	R
007	BNC2	non_synonymous	R52T	9	16727970	C	S
006	BOD1L	non_synonymous	G1895E	4	13602840	C	Y
148	BRAF	non_synonymous	K601N	7	140453132	T	W
279	BRAF	non_synonymous	D594G	7	140453154	T	Y

171	BRUNOL4	non_synonymous	F251L	18	34854324	A	R
785	BRUNOL4	splicing-site	-	18	34855076	T	C
282	BTBD16	non_synonymous	R343W	10	124090711	C	Y
136	BUD13	non_synonymous	R477C	11	116629055	G	R
117	BZRAP1	non_synonymous	A601S	17	56395712	C	M
040	C10orf71	non_synonymous	S1314Y	10	50534531	C	M
270	C10orf71	non_synonymous	L236F	10	50531296	C	Y
027	C10orf79	non_synonymous	V447M	10	105953730	C	Y
054	C10orf81	non_synonymous	V166I	10	115529621	G	R
136	C11orf57	non_synonymous	V280G	11	111953653	T	K
030	C12orf30	non_synonymous	L607F	12	112486157	G	R
194	C12orf40	non_synonymous	T481I	12	40110588	C	Y
189	C12orf51	non_synonymous	T2854P	12	112622944	T	K
006	C12orf64	non_synonymous	A613E	12	80764411	C	M
322	C12orf64	frameshift	V487fs	12	80752522	*	+T
008	C15orf42	non_synonymous	D904Y	15	90150044	G	K
191	C16orf14	non_synonymous	P141R	16	698129	C	S
191	C16orf57	non_synonymous	P37R	16	58036394	C	S
145	C17orf66	non_synonymous	P53S	17	34192382	G	R
156	C17orf67	non_synonymous	R60Q	17	54892279	C	Y
189	C1orf106	splicing-site	-	1	200869350	T	K
375	C1orf114	non_synonymous	D114E	1	169391327	G	K
322	C1orf125	frameshift	E990del2	1	179504034	*	-AAGAAC
100	C1orf128	frameshift	Y150del	1	24112827	*	-ATC
184	C1orf129	non_synonymous	R386C	1	170961432	C	Y
038	C1orf158	non_synonymous	R187P	1	12820859	G	S
761	C1QTNF1	non_synonymous	A105V	17	77042738	C	Y
321	C2	non_synonymous	S720N	6	31913034	G	R
148	C20orf100	frameshift	S398ins	20	42694558	*	+CCG
110	C20orf132	splicing-site	-	20	35802396	T	W
063	C20orf175	non_synonymous	R52*	20	49236638	G	R
091	C20orf194	non_synonymous	G320S	20	3321174	C	Y
170	C20orf200	non_synonymous	P75L	20	61143624	G	A
270	C20orf26	non_synonymous	L590F	20	20177382	C	Y
290	C20orf27	non_synonymous	V34E	20	3734771	A	W
052	C22orf13	frameshift	F109fs	22	24944012	*	-ACTC
007	C2orf16	non_synonymous	R994T	2	27802420	G	S
141	C2orf21	non_synonymous	A984V	2	210699644	C	Y
172	C2orf21	non_synonymous	D278G	2	210658478	A	R
051	C2orf44	non_synonymous	G230A	2	24261676	C	S
006	C3orf32	splicing-site	-	3	8669382	T	M
326	C3orf67	non_synonymous	V141D	3	58855954	A	W
090	C4orf43	non_synonymous	E110D	4	164436555	G	S
159	C5orf36	non_synonymous	K547R	5	93807258	T	Y
680	C6orf205	non_synonymous	P248T	6	30954694	C	C
033	C6orf25	non_synonymous	Q227*	6	31692785	C	Y
043	C6orf61	non_synonymous	V342A	6	119234465	A	R
270	C6orf89	non_synonymous	Q203*	6	36882360	C	Y
197	C7	non_synonymous	C702Y	5	40976882	G	R
110	C9orf103	non_synonymous	E199V	9	86258598	A	W

192	C9orf107	non_synonymous	I14T	9	105348041	T	Y
019	C9orf3	non_synonymous	R476C	9	97686329	C	Y
039	C9orf80	splicing-site	-	9	115456515	A	W
019	CACNA1A	non_synonymous	A405T	19	13443725	C	Y
274	CACNA1H	non_synonymous	F244L	16	1248703	C	S
083	CAGE1	non_synonymous	L650I	6	7370187	G	K
280	CALD1	non_synonymous	A26T	7	134613509	G	A
290	CAMK2B	non_synonymous	T623M	7	44259794	G	R
178	CAMK4	non_synonymous	Q147K	5	110730460	C	M
275	CAPN3	non_synonymous	I766T	15	42703115	T	Y
091	CARM1	non_synonymous	V167M	19	11019824	G	R
048	CASC1	non_synonymous	L648F	12	25261709	G	R
141	CASP1	non_synonymous	A317D	11	104899907	G	K
157	CBS	non_synonymous	E104D	21	44488623	C	M
159	CCBL1	non_synonymous	P208L	9	131600088	G	R
145	CCDC129	splicing-site	-	7	31683568	G	R
171	CCDC129	non_synonymous	F70Y	7	31594134	T	W
192	CCDC135	non_synonymous	L299Q	16	57741409	T	W
043	CCDC144A	non_synonymous	V1408I	17	16676891	G	R
017	CCDC158	splicing-site	-	4	77290577	T	M
680	CCDC59	non_synonymous	Q180K	12	82748300	G	K
053	CCDC63	non_synonymous	I182T	12	111317765	T	Y
325	CCDC73	non_synonymous	V505I	11	32636351	C	Y
185	CCDC82	non_synonymous	Q386*	11	96104230	G	R
049	CCNA2	frameshift	L376fs	4	122739321	*	-A
189	CCNI	non_synonymous	N349Y	4	77969461	T	W
178	CCT6B	non_synonymous	V87I	17	33285656	C	Y
178	CD163	non_synonymous	W1117*	12	7633750	C	Y
181	CD36	non_synonymous	F266L	7	80299318	C	M
273	CD36	non_synonymous	G287*	7	80300333	G	K
064	CD74	non_synonymous	R10W	5	149792285	G	R
091	CD99L2	non_synonymous	A84D	X	149997957	G	K
282	CDC14B	splicing-site	-	9	99301359	G	Y
319	CDC2L2	non_synonymous	D655E	1	1571841	A	M
141	CDC2L5	non_synonymous	T876A	7	40102450	A	R
174	CDC5L	non_synonymous	E553*	6	44394225	G	K
110	CDCP1	non_synonymous	S523R	3	45134827	G	K
043	CDH11	non_synonymous	H464Y	16	65006807	G	R
018	CDH18	non_synonymous	A723V	5	19473540	G	R
008	CDH23	non_synonymous	N3094S	10	73571125	A	R
192	CDH23	non_synonymous	R476H	10	73405724	G	R
761	CDH23	non_synonymous	S486N	10	73406232	G	R
091	CDH3	non_synonymous	D373G	16	68716326	A	R
290	CDH7	non_synonymous	N547K	18	63527033	C	S
324	CDH9	non_synonymous	F316I	5	26903799	A	W
009	CEACAM1	splicing-site	-	19	43016500	T	M
155	CENPI	non_synonymous	K625N	X	100402800	G	S
194	CEP350	non_synonymous	A2491T	1	180062711	G	R
030	CEP57	non_synonymous	G341S	11	95561085	G	R
184	CFH	non_synonymous	V72I	1	196642263	G	R

618	CFHR4	non_synonymous	A540P	1	196887417	G	S
156	CGN	non_synonymous	P5A	1	151491008	C	S
007	CHD2	splicing-site	-	15	93552555	T	K
043	CHD2	non_synonymous	L1270F	15	93540558	G	K
175	CHD2	frameshift	L698fs	15	93510647	*	-C
181	CHD2	non_synonymous	F1146L	15	93534730	T	K
185	CHD2	non_synonymous	H620L	15	93499738	A	W
063	CHKB	non_synonymous	Q360R	22	51017889	T	Y
170	CHMP2B	non_synonymous	*214S	3	87302971	A	M
054	CHSY1	frameshift	D589fs	15	101718235	*	-TCTC
275	CLASP2	non_synonymous	Q759H	3	33623383	T	K
156	CLC	splicing-site	-	19	40228577	G	Y
110	CLDN15	non_synonymous	A98V	7	100877648	G	R
290	CLDN2	non_synonymous	A137V	X	106171868	C	Y
272	CLEC2A	non_synonymous	R17Q	12	10084879	C	Y
375	CLMN	non_synonymous	A934T	14	95660226	C	Y
785	CLPTM1	non_synonymous	K172R	19	45480646	A	R
117	CLSTN3	non_synonymous	M785I	12	7303249	G	K
064	CLU	non_synonymous	Q307H	8	27462505	C	M
194	CNOT3	non_synonymous	E70K	19	54647435	G	R
146	CNTN4	non_synonymous	A602V	3	3076337	C	Y
328	CNTN6	non_synonymous	G664V	3	1415653	G	K
157	COG4	non_synonymous	V689F	16	70515708	C	M
022	COG5	non_synonymous	L478V	7	106924152	G	S
005	COL22A1	non_synonymous	R582C	8	139790610	G	R
324	COL22A1	non_synonymous	V1179I	8	139649005	C	Y
054	COL25A1	non_synonymous	D289N	4	109817864	C	Y
194	COL25A1	non_synonymous	D516E	4	109766375	A	W
006	COL4A3	non_synonymous	C1551R	2	228173930	T	Y
007	COL4A4	non_synonymous	R227P	2	227973562	C	S
155	COL4A6	non_synonymous	G540E	X	107431229	C	Y
178	COL8A2	non_synonymous	G281*	1	36564441	C	M
155	COQ5	non_synonymous	R92H	12	120960094	C	Y
157	CORO1C	non_synonymous	T485R	12	109042391	G	S
159	CPEB3	non_synonymous	D502N	10	93870901	C	Y
008	CPNE4	non_synonymous	N279I	3	131300454	T	W
279	CPVL	non_synonymous	I151F	7	29134711	T	W
618	CR392039.3	non_synonymous	A86T	21	9909079	C	Y
270	CRAT	non_synonymous	A481P	9	131860315	C	S
282	CREB1	non_synonymous	R284*	2	208442348	C	Y
181	CRELD1	non_synonymous	G167R	3	9982572	G	R
064	CRNN	non_synonymous	R125H	1	152383072	C	Y
042	CROT	non_synonymous	F349I	7	87006749	T	W
321	CRY1	non_synonymous	R367*	12	107393367	G	R
186	CSMD1	non_synonymous	R1013*	8	3165305	G	R
278	CSMD1	non_synonymous	P1759T	8	3000128	G	K
273	CSMD2	non_synonymous	V733I	1	34204792	C	Y
043	CSMD3	non_synonymous	V3694E	8	113237043	A	W
117	CSMD3	non_synonymous	P2402H	8	113332171	G	K
168	CSMD3	non_synonymous	E1838D	8	113420638	T	K

279	CSMD3	non_synonymous	A2358T	8	113347651	C	Y
052	CSN2	non_synonymous	E201*	4	70823066	C	M
091	CSTF2	non_synonymous	P255L	X	100081684	C	Y
117	CTBP2	non_synonymous	A966G	10	126678148	G	S
191	CTH	non_synonymous	T308R	1	70899556	C	S
030	CTNNA2	non_synonymous	E87V	2	79971670	A	W
006	CTNNA3	non_synonymous	K855E	10	67680213	T	Y
178	CTNND2	non_synonymous	N1166K	5	10973745	A	M
273	CTSH	non_synonymous	S97P	15	79228033	A	R
006	CTSO	non_synonymous	S249N	4	156850786	C	Y
144	CUBN	non_synonymous	V2901I	10	16932424	C	Y
197	CXorf22	non_synonymous	S505W	X	35984785	C	S
090	CXorf41	non_synonymous	E9Q	X	106456130	G	S
171	CYFIP1	non_synonymous	P1237T	15	23002981	C	M
023	CYFIP2	non_synonymous	V745I	5	156757751	G	R
007	CYHR1	non_synonymous	W141S	8	145689667	C	S
170	CYorf15A	non_synonymous	I123V	Y	21751494	A	R
618	CYP11B1	non_synonymous	P434L	8	143957161	G	R
019	CYP2A7	non_synonymous	R381Q	19	41383114	C	Y
188	CYP3A43	non_synonymous	M358L	7	99459281	A	W
280	CYP51A1	non_synonymous	R452H	7	91743154	C	Y
192	CYP8B1	non_synonymous	Q486*	3	42915853	G	R
136	CYTH4	splicing-site	-	22	37693603	A	M
194	DCAF4L2	non_synonymous	V213M	8	88885563	C	Y
186	DCT	non_synonymous	L322V	13	95114343	A	M
006	DDAH1	non_synonymous	G270R	1	85787185	C	Y
375	DDX11L8	non_synonymous	S409R	12	9453821	C	M
188	DDX3X	non_synonymous	M330K	X	41203616	T	W
328	DDX3X	non_synonymous	S410F	X	41204715	C	Y
375	DDX52	non_synonymous	K73N	17	36002206	T	W
280	DDX54	splicing-site	-	12	113607573	T	R
091	DDX58	non_synonymous	E758K	9	32466353	C	Y
323	DDX6	non_synonymous	T266M	11	118630698	G	R
146	DENND1A	non_synonymous	L596F	9	126145984	G	R
174	DEPDC1B	non_synonymous	R158G	5	59941425	G	S
197	DHRS7B	non_synonymous	K183*	17	21087704	A	W
030	DHX36	non_synonymous	Y197C	3	154032848	T	Y
054	DIAPH3	non_synonymous	L845P	13	60453436	A	R
171	DIO2	non_synonymous	S85G	14	80669601	T	Y
041	DLC1	non_synonymous	S744T	8	12957615	C	S
267	DLC1	non_synonymous	N251S	8	13356829	T	Y
375	DLEC1	non_synonymous	V944I	3	38141882	G	R
178	DLG2	non_synonymous	R10C	11	83362897	G	R
188	DLG5	non_synonymous	V706M	10	79589182	C	Y
270	DLK1	non_synonymous	A249V	14	101200827	C	Y
324	DMD	non_synonymous	L341M	X	32663209	G	T
090	DMXL2	non_synonymous	P1924S	15	51773533	G	R
758	DNAH17	non_synonymous	C3228Y	17	76455219	C	Y
044	DNAH3	non_synonymous	A2694V	16	20986733	G	R
083	DNAH5	non_synonymous	R529W	5	13911554	G	R

197	DNAH6	non_synonymous	P966T	2	84831490	C	M
193	DNAH7	splicing-site	-	2	196661298	T	R
009	DNAH8	non_synonymous	G1547E	6	38813489	G	R
321	DNAH9	splicing-site	-	17	11572379	A	M
264	DNAJC28	non_synonymous	T197M	21	34861111	G	R
174	DNM1	non_synonymous	V659L	9	131010931	G	S
006	DOCK1	non_synonymous	E1608K	10	129216800	G	R
051	DOCK4	non_synonymous	T622A	7	111512387	T	Y
282	DOCK4	non_synonymous	T1126R	7	111428742	G	S
279	DPCR1	non_synonymous	H924L	6	30919012	A	W
282	DPEP1	splicing-site	-	16	89703790	T	T
110	DPF2	non_synonymous	P222L	11	65113164	C	Y
266	DPP6	non_synonymous	G269W	7	154519519	G	K
323	DPP6	non_synonymous	A317T	7	154561192	G	R
192	DRP2	non_synonymous	A520V	X	100505430	C	Y
018	DSC3	non_synonymous	Q157R	18	28609479	T	Y
785	DSCAML1	non_synonymous	V179I	11	117651217	C	Y
038	DSE	non_synonymous	G543E	6	116757259	G	R
171	DSG2	non_synonymous	K275Q	18	29104543	A	M
758	DSG3	non_synonymous	A527T	18	29046660	G	R
018	DST	non_synonymous	V5572F	6	56394500	C	M
171	DST	non_synonymous	E2090*	6	56484190	C	M
013	DTNA	non_synonymous	E753Q	18	32462127	G	S
170	DTNA	non_synonymous	R703*	18	32459628	C	Y
052	DTX1	non_synonymous	W30*	12	113496087	G	R
642	DTX2	non_synonymous	F244S	7	76112287	T	Y
016	DUOXA1	non_synonymous	V431A	15	45409873	A	R
045	DYNC1H1	non_synonymous	L3761F	14	102505414	G	S
186	DYNC2H1	non_synonymous	Q3615R	11	103153747	A	R
044	ECE2	non_synonymous	S672N	3	184008350	G	R
322	ECHDC3	non_synonymous	V193I	10	11797434	G	R
325	EDAR	non_synonymous	C333Y	2	109524377	C	Y
022	EEF1A1	non_synonymous	G70A	6	74229175	C	S
194	EFHA2	non_synonymous	R316H	8	16956025	G	R
082	EGFR	non_synonymous	D1168N	7	55273179	G	R
618	EGFR	non_synonymous	V323I	7	55223600	G	A
181	EGR1	non_synonymous	E37K	5	137801559	G	R
082	EGR2	non_synonymous	H384N	10	64573248	G	K
290	EGR2	non_synonymous	E356K	10	64573332	C	Y
280	EHD4	splicing-site	-	15	42211822	A	K
324	EIF4A3	non_synonymous	I141L	17	78113891	T	K
052	ELAVL2	non_synonymous	L243R	9	23701446	A	M
280	EMR4P	non_synonymous	A209T	19	6971308	C	Y
124	ENPP6	non_synonymous	R82H	4	185074883	C	Y
032	ENTPD4	non_synonymous	Y429C	8	23294535	T	Y
090	EP300	non_synonymous	C1790G	22	41573083	T	K
188	EPB41L4A	non_synonymous	R246Q	5	111594984	C	Y
194	EPHA6	non_synonymous	E735K	3	97251204	G	R
064	EPHA7	non_synonymous	S684I	6	93967876	C	M
178	EPHB1	non_synonymous	R364Q	3	134851685	G	R

270	EPHB1	non_synonymous	V760A	3	134920464	T	Y
030	ERBB4	non_synonymous	T475P	2	212566758	T	K
280	ERF	non_synonymous	W67G	19	42754541	A	M
166	ERICH1	non_synonymous	E193K	8	623775	C	Y
328	ETAA1	non_synonymous	P17R	2	67624630	C	S
282	EXOC3L	splicing-site	-	16	67221742	A	Y
192	EXOC4	non_synonymous	T485K	7	133314834	C	M
041	EXOC6B	non_synonymous	G713C	2	72562135	C	M
785	EXT2	non_synonymous	R427Q	11	44193237	G	R
039	EYA1	non_synonymous	Q119L	8	72234031	T	W
758	FAM114A2	non_synonymous	R340I	5	153382525	C	M
185	FAM117A	non_synonymous	E133*	17	47799926	C	M
324	FAM117A	non_synonymous	S274F	17	47794964	G	R
039	FAM120B	non_synonymous	T558P	6	170628150	A	M
039	FAM120B	non_synonymous	V560G	6	170628157	T	K
193	FAM122C	non_synonymous	T133A	X	133986881	A	R
321	FAM13A	non_synonymous	R649Q	4	89671055	C	Y
290	FAM190A	non_synonymous	E664Q	4	91645122	G	S
264	FAM22G	non_synonymous	P308L	9	99698787	C	T
323	FAM47B	non_synonymous	G585C	X	34962701	G	K
175	FAM5C	non_synonymous	I486V	1	190067993	T	Y
168	FANCD2	splicing-site	-	3	10106560	G	K
033	FANCE	splicing-site	-	6	35428397	T	K
272	FANCM	non_synonymous	C1819W	14	45665491	T	K
272	FANCM	non_synonymous	S1869T	14	45665639	T	W
148	FAT1	non_synonymous	T3145M	4	187534301	G	R
618	FAT3	non_synonymous	C8S	11	92085300	T	W
761	FAT3	non_synonymous	F193L	11	92085857	C	S
194	FBF1	non_synonymous	H470Q	17	73918150	G	K
267	FBLN2	non_synonymous	A891T	3	13670506	G	R
030	FBN1	non_synonymous	N2740S	15	48704773	T	Y
043	FBN1	non_synonymous	A2086S	15	48730022	C	M
181	FBN2	non_synonymous	C132Y	5	127866329	C	Y
618	FBN2	non_synonymous	R1237L	5	127671694	C	M
680	FBN3	non_synonymous	T1105M	19	8183804	G	R
027	FBXL13	splicing-site	-	7	102608566	A	W
016	FBXL16	non_synonymous	N269S	16	745751	T	Y
321	FBXL7	non_synonymous	R306Q	5	15936877	G	R
618	FBXO17	splicing-site	-	19	39412308	G	S
045	FBXO28	non_synonymous	R363C	1	224345428	C	Y
054	FBXW10	non_synonymous	C608F	17	18671878	G	K
194	FCRL1	non_synonymous	Y168S	1	157772271	T	K
194	FCRL1	non_synonymous	T165A	1	157772281	T	Y
124	FGD3	non_synonymous	A190V	9	95766308	C	Y
178	FGF10	non_synonymous	V33I	5	44388688	C	Y
064	FGFR2	non_synonymous	Y350N	10	123276935	A	W
278	FGFR2	non_synonymous	D491N	10	123263332	C	Y
375	FGG	non_synonymous	C24S	4	155533692	A	W
141	FGL1	non_synonymous	R88C	8	17739640	G	R
019	FHAD1	non_synonymous	S1321C	1	15708528	A	W

039	FHDC1	splicing-site	-	4	153881715	A	W
090	FHL1	non_synonymous	S260P	X	135292071	T	Y
048	FHOD3	non_synonymous	K943M	18	34298614	A	W
090	FILIP1L	non_synonymous	K779Q	3	99568185	T	K
168	FKBP8	splicing-site	-	19	18652487	T	M
043	FLNB	splicing-site	-	3	58109419	T	K
185	FLOT1	non_synonymous	I249T	6	30698855	A	R
083	FLRT2	non_synonymous	T380S	14	86088996	A	W
032	FNDC1	non_synonymous	W1678*	6	159672533	G	R
272	FNIP2	non_synonymous	E1016V	4	159812626	A	W
758	FOXD4L2	frameshift	C405fs	9	42719279	*	-C
152	FOXD4L4	frameshift	*417del	9	70427649	*	-CAG
290	FOXP3	non_synonymous	Q407L	X	49107946	T	W
144	FRMD3	non_synonymous	S509L	9	85863101	G	R
049	FRMPD4	non_synonymous	K38N	X	12627915	G	S
144	FRYL	non_synonymous	V2450G	4	48525090	A	M
029	FSD1L	non_synonymous	I26V	9	108223861	A	R
182	FSHB	non_synonymous	G83S	11	30255204	G	R
264	FSTL5	non_synonymous	V581L	4	162376256	C	M
280	FSTL5	non_synonymous	S401R	4	162459427	G	K
016	FUBP1	non_synonymous	Q541*	1	78425887	G	R
270	FUBP1	non_synonymous	G140*	1	78432628	C	M
145	FUT1	non_synonymous	V206F	19	49254292	C	M
282	GABRA5	non_synonymous	C173Y	15	27159970	G	R
064	GAD1	non_synonymous	R90C	2	171686107	C	Y
194	GALK2	non_synonymous	R39*	15	49493420	C	Y
159	GALNT11	non_synonymous	R549W	7	151818003	C	Y
027	GALNT2	non_synonymous	L421P	1	230398700	T	Y
159	GALNT8	non_synonymous	H121Y	12	4835847	C	Y
274	GARNL1	non_synonymous	M2060V	14	36008822	T	Y
007	GAS2L3	non_synonymous	P442R	12	101017908	C	S
013	GBP2	splicing-site	-	1	89582674	G	Y
083	GCN1L1	non_synonymous	R2649*	12	120565724	G	R
030	GCSH	non_synonymous	R51H	16	81124282	C	Y
270	GDF9	non_synonymous	M446T	5	132197309	A	R
157	GFRA2	non_synonymous	Q227K	8	21608215	G	K
006	GJB5	non_synonymous	R32H	1	35223026	G	R
272	GJD2	non_synonymous	R108C	15	35045323	G	R
145	GLI1	non_synonymous	G819A	12	57864979	G	S
758	GLI2	non_synonymous	Y259*	2	121726423	C	M
006	GNAI1	non_synonymous	A101V	7	79818546	C	Y
136	GNAT1	non_synonymous	A83T	3	50230795	G	R
282	GNAT1	splicing-site	-	3	50231184	A	C
278	GPC6	non_synonymous	P366S	13	94958321	C	Y
194	GPR1	non_synonymous	H204Q	2	207041360	A	W
680	GPR112	non_synonymous	L418P	X	135427118	T	Y
032	GPR98	non_synonymous	T2017P	5	89979787	A	M
642	GPRC5B	non_synonymous	T33S	16	19884071	T	W
192	GPS2	non_synonymous	Q192*	17	7216947	G	A
136	GRIK3	non_synonymous	D733N	1	37271822	C	Y



266	GRIK5	non_synonymous	Y130S	19	42566759	T	K
270	GRLF1	non_synonymous	N1099S	19	47425228	A	R
013	GRM1	non_synonymous	A184T	6	146351203	G	R
185	GRM3	non_synonymous	R723W	7	86468997	C	Y
144	GRM5	non_synonymous	E250D	11	88718018	T	K
282	GRM7	non_synonymous	R260H	3	7340413	G	R
027	GRM8	non_synonymous	L626P	7	126173559	A	R
027	GRM8	non_synonymous	N480S	7	126249471	T	Y
165	GRWD1	frameshift	D123del	19	48950001	*	-GAA
280	GTF2IRD1	splicing-site	-	7	73959134	T	K
680	GUCY1A2	non_synonymous	E729V	11	106558381	T	W
172	GUCY2D	non_synonymous	R331P	17	7907440	G	C
016	H2AFY2	non_synonymous	T36M	10	71835521	C	Y
273	HAO1	non_synonymous	V367F	20	7864254	C	M
184	HCN1	non_synonymous	T820M	5	45262237	G	R
043	HDAC9	frameshift	V1037fs	7	19015515	*	+T
267	HEATR7B1	non_synonymous	I932T	2	234722366	T	Y
274	HECW1	non_synonymous	R1256*	7	43546774	C	Y
051	HERC3	non_synonymous	G189E	4	89574122	G	R
290	HGF	non_synonymous	R468H	7	81346550	C	Y
054	HHIP	non_synonymous	D513N	4	145635490	G	R
006	HHLA2	non_synonymous	I14V	3	108070700	A	R
117	HIST1H1B	non_synonymous	A137G	6	27834898	G	S
051	HIST1H1D	non_synonymous	S90N	6	26234893	C	Y
091	HIST1H1E	non_synonymous	A65P	6	26156811	G	C
110	HIST1H2BO	non_synonymous	I40M	6	27861360	C	S
280	HIST2H2AC	non_synonymous	G5D	1	149858538	G	R
191	HIST2H2BE	non_synonymous	S37R	1	149858080	G	S
178	HIST4H4	non_synonymous	G95S	12	14923736	C	Y
020	HIVEP1	non_synonymous	S1572C	6	12124743	C	S
319	HIVEP2	non_synonymous	V1043I	6	143092749	C	Y
007	HLA-DRB5	non_synonymous	N149S	6	32487353	T	Y
124	HMCN1	non_synonymous	R4475H	1	186105911	G	R
195	HMCN1	non_synonymous	T3811A	1	186084416	A	R
157	HMCN2	non_synonymous	R394*	9	133303780	C	Y
039	HMGCLL1	non_synonymous	L335F	6	55304240	G	R
170	HNMT	non_synonymous	T27M	2	138722141	C	Y
186	HOXD13	non_synonymous	K303N	2	176959335	G	K
174	HPS4	non_synonymous	G231E	22	26862070	C	Y
083	HPSE2	non_synonymous	Y544*	10	100221558	G	K
029	HRNR	non_synonymous	R547*	1	152192466	G	R
194	HSF5	non_synonymous	G436V	17	56540378	C	M
041	HSPG2	non_synonymous	L2965P	1	22169279	A	R
323	HSPH1	non_synonymous	I809V	13	31711613	T	Y
009	HTR3B	non_synonymous	M288T	11	113813870	T	Y
168	HYAL4	non_synonymous	Q114K	7	123508667	C	M
018	HYDIN	non_synonymous	H4269Y	16	70883694	G	R
091	HYDIN	frameshift	Q3904fs	16	70896015	*	-A
181	HYDIN	non_synonymous	I3028F	16	70929947	T	W
761	HYDIN	non_synonymous	N2468S	16	70954873	T	Y

043	IGF1R	non_synonymous	A1206T	15	99491831	G	R
785	IGLV3-1	non_synonymous	Y98S	22	23235963	A	M
008	IGSF10	non_synonymous	M1190K	3	151164200	A	W
178	IGSF9B	non_synonymous	P982L	11	133790675	G	A
013	IKZF3	non_synonymous	L162R	17	37947776	A	M
272	IL17RC	splicing-site	-	3	9970172	T	Y
186	IL33	non_synonymous	Q34K	9	6250482	C	M
276	IL8	non_synonymous	D79E	4	74607702	C	M
325	ILVBL	splicing-site	-	19	15226484	A	K
189	IMPG2	non_synonymous	S1144R	3	100948427	T	K
175	INVS	non_synonymous	K310I	9	103008920	A	W
194	IQCE	non_synonymous	S95*	7	2611850	C	S
188	IQGAP2	non_synonymous	R982H	5	75967685	G	R
181	IRAK1	non_synonymous	L692F	X	153277986	G	A
157	IRF4	non_synonymous	S114R	6	394946	C	M
278	ISX	non_synonymous	Q74L	22	35463301	A	W
016	ITGA2B	non_synonymous	A164V	17	42463002	G	R
052	ITGA2B	splicing-site	-	17	42461451	T	C
027	ITK	non_synonymous	K119E	5	156641231	A	R
282	ITPRIPL1	non_synonymous	T85P	2	96992598	A	M
019	JMJD4	non_synonymous	Q451*	1	227920134	G	R
758	JSRP1	non_synonymous	E9K	19	2255289	C	T
136	KALRN	non_synonymous	V743D	3	124117606	T	W
273	KANK3	splicing-site	-	19	8399382	T	M
290	KATNAL1	non_synonymous	R290C	13	30805468	G	R
146	KCNA10	non_synonymous	V417I	1	111060161	C	Y
038	KCNA4	non_synonymous	L589F	11	30032461	G	R
032	KCNAB1	non_synonymous	G132A	3	156175279	G	S
273	KCNAB1	non_synonymous	A41V	3	155861089	C	Y
039	KCNC4	non_synonymous	G333S	1	110765904	G	R
064	KCNH7	non_synonymous	L413R	2	163302844	A	M
007	KCNH8	non_synonymous	K90I	3	19295338	A	W
064	KCNT2	non_synonymous	Y279N	1	196397384	A	W
184	KCTD5	non_synonymous	L202P	16	2752409	T	Y
278	KDM2B	non_synonymous	H799R	12	121881870	T	Y
761	KDM5A	non_synonymous	D920Y	12	427411	C	M
007	KIAA0146	non_synonymous	P24S	8	48192486	C	Y
185	KIAA0284	non_synonymous	V1542M	14	105361146	G	R
029	KIAA0586	frameshift	Q1512fs	14	58979291	*	-AA
016	KIAA0892	splicing-site	-	19	19431945	G	R
189	KIAA0913	non_synonymous	V1308I	10	75557813	G	R
029	KIAA0947	non_synonymous	G548*	5	5461089	G	K
181	KIAA1033	non_synonymous	M495V	12	105534102	A	R
044	KIAA1217	non_synonymous	R1188W	10	24831649	C	Y
029	KIAA1377	non_synonymous	S547Y	11	101833406	C	M
191	KIAA1486	non_synonymous	C292S	2	226447007	T	W
165	KIAA1543	non_synonymous	D1251N	19	7682863	G	R
032	KIAA1632	non_synonymous	L776P	18	43510727	A	R
155	KIAA1632	frameshift	L1146fs	18	43496118	*	-A
052	KIAA1881	non_synonymous	A397G	19	4512740	G	S

090	KIAA2018	splicing-site	-	3	113383158	T	R
141	KIF13B	splicing-site	-	8	29120495	T	M
181	KIF18B	splicing-site	-	17	43003780	T	M
083	KIF1A	non_synonymous	S1699P	2	241658566	A	R
267	KIF26B	non_synonymous	A188T	1	245530232	G	R
009	KIF5A	non_synonymous	R718W	12	57970115	C	Y
270	KIF5C	non_synonymous	V484L	2	149837956	G	S
033	KIT	non_synonymous	V833L	4	55602676	G	S
016	KLHL17	non_synonymous	L298Q	1	897609	T	W
030	KRIT1	non_synonymous	V710E	7	91830634	A	W
159	KRT1	non_synonymous	I312T	12	53071462	A	R
039	KRT2	non_synonymous	R341H	12	53042057	C	Y
051	KRT6B	non_synonymous	R182W	12	52844401	G	R
148	KRTAP10-6	non_synonymous	V230M	21	46011678	C	Y
165	LAMA3	non_synonymous	D918V	18	21407355	A	W
051	LAMB1	non_synonymous	A843T	7	107600067	C	Y
064	LAMB4	non_synonymous	N589K	7	107720166	G	K
618	LARP1B	non_synonymous	V631I	4	129099792	G	R
018	LAT2	non_synonymous	R123W	7	73636001	C	Y
032	LBA1	non_synonymous	E1791G	3	36879876	T	Y
680	LCAP	non_synonymous	D144E	X	153153991	C	S
267	LCMT2	non_synonymous	Y193C	15	43622110	T	C
266	LCN10	splicing-site	-	9	139635815	A	W
192	LEFTY2	non_synonymous	T296P	1	226125356	T	K
117	LEMD3	non_synonymous	L703F	12	65634001	A	M
110	LEO1	non_synonymous	D665E	15	52230359	A	W
019	LIPG	non_synonymous	V269M	18	47107796	G	R
156	LMTK2	non_synonymous	T840I	7	97822296	C	Y
761	LNPEP	non_synonymous	D372G	5	96322358	A	R
063	LPHN2	non_synonymous	A1066T	1	82447514	G	R
192	LPHN2	non_synonymous	T848S	1	82434892	A	W
053	LPHN3	non_synonymous	W273R	4	62598894	T	W
082	LPHN3	non_synonymous	P70H	4	62453098	C	M
091	LPHN3	non_synonymous	A652V	4	62800643	C	Y
184	LRIG3	non_synonymous	V811M	12	59271287	C	Y
178	LRIT1	non_synonymous	V538I	10	85991943	C	Y
023	LRP1	non_synonymous	R1281C	12	57569739	C	Y
022	LRP12	non_synonymous	R429H	8	105509494	C	Y
005	LRP1B	non_synonymous	C2205F	2	141458115	C	M
274	LRP1B	non_synonymous	S3352P	2	141214044	A	R
276	LRP1B	non_synonymous	Y4436F	2	141027862	T	W
322	LRP1B	non_synonymous	C2567S	2	141294203	C	S
326	LRP1B	non_synonymous	V3150I	2	141243000	C	Y
145	LRP2	non_synonymous	R3646H	2	170030506	C	Y
184	LRP5	non_synonymous	A65V	11	68115417	C	Y
054	LRP6	non_synonymous	R360C	12	12334272	G	R
054	LRRC2	non_synonymous	V229I	3	46571483	C	Y
184	LRRC4	splicing-site	-	7	127670795	A	K
680	LRRC41	non_synonymous	Q638E	1	46745906	G	S
170	LRRC52	non_synonymous	L103H	1	165513841	T	W

146	LRRRC6	non_synonymous	R11W	8	133673853	G	R
053	LRRFIP2	non_synonymous	R450Q	3	37116537	C	Y
185	LTB	splicing-site	-	6	31549590	G	M
032	LTBP1	non_synonymous	P669S	2	33477749	C	Y
045	LTBP4	splicing-site	-	19	41119946	T	G
170	LUZP2	non_synonymous	M206I	11	25004692	G	K
290	LUZP2	non_synonymous	R241G	11	25004795	A	R
136	LYST	non_synonymous	S1840L	1	235938328	G	R
194	MAGEB1	non_synonymous	L236F	X	30269318	A	M
174	MAGEB6	non_synonymous	P103L	X	26212271	C	Y
171	MAGEC1	non_synonymous	Q32K	X	140993284	C	M
083	MAGEH1	non_synonymous	W197*	X	55479398	G	R
188	MAGOH	non_synonymous	D43E	1	53701267	A	W
785	MAL	splicing-site	-	2	95713702	A	C
168	MAN2B1	splicing-site	-	19	12768875	T	M
761	MAP2K2	non_synonymous	Q60P	19	4117541	T	K
375	MAP3K15	non_synonymous	F1058L	X	19389585	A	G
185	MAP4K4	non_synonymous	N577K	2	102477313	C	M
193	MAP7	non_synonymous	E431K	6	136686921	C	Y
194	MARS	non_synonymous	C12W	12	57881909	C	S
159	MATK	non_synonymous	A203V	19	3783195	G	R
155	MBNL2	splicing-site	-	13	98009104	G	R
174	MBTPS1	non_synonymous	G790R	16	84099358	C	Y
186	MDGA2	non_synonymous	R53W	14	47770670	G	R
159	MDN1	non_synonymous	L2900V	6	90409954	G	S
278	MED12	non_synonymous	L36R	X	70339230	T	G
282	MED12	non_synonymous	G44S	X	70339253	G	R
008	MEGF9	non_synonymous	I399V	9	123374677	T	Y
171	MFN1	non_synonymous	N602I	3	179103415	A	W
019	MGAT4B	non_synonymous	H427N	5	179226037	G	K
328	MGAT5	non_synonymous	Q563R	2	135180384	A	R
322	MGMT	splicing-site	-	10	131565050	A	M
168	MIA	non_synonymous	Q131R	19	41283321	A	R
019	MICALCL	non_synonymous	C114Y	11	12315319	G	R
030	MID1	non_synonymous	R36C	X	10535482	G	A
146	MINK1	splicing-site	-	17	4794810	G	R
172	MIOS	non_synonymous	P767R	7	7635991	C	S
039	MKL1	non_synonymous	E816G	22	40807746	T	C
032	MLLT3	non_synonymous	A313T	9	20413907	C	Y
141	MMEL1	non_synonymous	R246W	1	2537701	G	R
049	MNDA	non_synonymous	L367V	1	158817629	C	S
048	MOAP1	non_synonymous	M15T	14	93650544	A	R
045	MPDZ	non_synonymous	V1950A	9	13110044	A	R
189	MPHOSPH10	non_synonymous	I31S	2	71360030	T	K
038	MRGPRE	non_synonymous	E32K	11	3249936	C	Y
054	MRPL3	non_synonymous	D54E	3	131220699	G	K
642	MRPS6	non_synonymous	E106G	21	35514839	A	R
019	MSI2	splicing-site	-	17	55334826	G	S
157	MUC16	non_synonymous	R2782T	19	9083470	C	S
159	MUC16	non_synonymous	L4137V	19	9075037	G	S

039	MUC17	non_synonymous	T3350R	7	100684746	C	S
017	MUC2	non_synonymous	T1728S	11	1093364	C	S
267	MUC2	non_synonymous	T1744M	11	1093412	C	Y
290	MUC2	non_synonymous	T1702S	11	1093286	C	S
322	MUC2	non_synonymous	T1564S	11	1092872	C	S
007	MUC4	non_synonymous	P4050T	3	195506303	G	K
680	MUC4	non_synonymous	S448C	3	195517108	G	S
159	MUC5B	non_synonymous	T4887M	11	1271225	C	Y
100	MYCT1	non_synonymous	R127H	6	153043060	G	R
181	MYD88	non_synonymous	L265P	3	38182641	T	Y
785	MYD88	non_synonymous	L265P	3	38182641	T	Y
197	MYH1	non_synonymous	R1348W	17	10402082	G	R
266	MYH13	non_synonymous	A1762V	17	10210266	G	R
090	MYH2	non_synonymous	H1934D	17	10424623	G	S
279	MYH8	non_synonymous	R26P	17	10323468	C	S
009	MYO1B	non_synonymous	R96*	2	192194695	C	Y
275	MYOG	non_synonymous	G88R	1	203054903	C	S
027	NAALADL2	non_synonymous	G60D	3	174814715	G	R
148	NALCN	non_synonymous	R372C	13	101936304	G	R
280	NALCN	non_synonymous	H464R	13	101890149	T	Y
043	NAV2	non_synonymous	T1810P	11	20101690	A	M
063	NBEAL1	non_synonymous	I2350V	2	204064067	A	R
045	NBPF14	non_synonymous	S844I	1	148004783	C	M
053	NCBP2	non_synonymous	S161Y	3	196664391	G	K
178	NCR2	non_synonymous	P195L	6	41309767	C	Y
185	NCRNA00164	non_synonymous	R242H	2	132911157	C	Y
041	NF1	non_synonymous	R2594P	17	29684020	G	S
110	NF1	non_synonymous	K1444N	17	29585520	G	S
174	NFAT5	non_synonymous	E214A	16	69681318	A	M
016	NFKBIE	non_synonymous	E285*	6	44230329	C	M
020	NHS	non_synonymous	L215P	X	17705940	T	Y
029	NKAP	non_synonymous	Y406*	X	119059213	G	S
136	NLE1	non_synonymous	V345G	17	33462448	A	M
156	NLN	frameshift	K693fs	5	65118706	*	-AG
197	NLN	non_synonymous	A481V	5	65088397	C	Y
090	NLRC4	non_synonymous	H797Y	2	32463333	G	R
178	NLRP4	non_synonymous	L483F	19	56370208	G	K
006	NLRP5	non_synonymous	V239M	19	56538314	G	R
009	NOD1	non_synonymous	S376G	7	30491907	T	Y
267	NOL8	non_synonymous	D945G	9	95068110	T	Y
186	NOP56	non_synonymous	I262R	20	2636268	T	K
272	NPAT	non_synonymous	I672V	11	108043697	T	Y
013	NPBWR2	non_synonymous	T78M	20	62737952	G	A
280	NPEPL1	non_synonymous	R474G	20	57290230	C	S
029	NPFFR2	non_synonymous	V239A	4	73003838	T	Y
275	NPHP1	non_synonymous	Q360K	2	110919224	G	K
145	NPHP4	non_synonymous	V312L	1	6008188	C	M
124	NPS	non_synonymous	Y37H	10	129350742	T	Y
270	NRG1	non_synonymous	V489M	8	32621438	G	R
155	NRG2	non_synonymous	V358I	5	139251346	C	Y

141	NRG3	non_synonymous	D586H	10	84744954	G	S
016	NSD1	non_synonymous	T2029A	5	176710863	A	R
185	NTF3	non_synonymous	R107Q	12	5603661	G	R
197	NTRK2	non_synonymous	A199T	9	87338499	G	R
174	NUDT21	non_synonymous	D72G	16	56481803	T	Y
189	NUSAP1	non_synonymous	E7K	15	41625174	G	R
023	NXF1	non_synonymous	K22*	11	62571415	T	W
082	NXF1	non_synonymous	R78*	11	62571028	G	R
083	NXF1	non_synonymous	L212R	11	62569215	A	M
186	NXN	non_synonymous	R220Q	17	725651	C	Y
761	NXPH4	non_synonymous	P273L	12	57619421	C	T
040	ODZ1	non_synonymous	C1110R	X	123637527	A	R
117	ODZ1	non_synonymous	K2174E	X	123518261	T	Y
013	ODZ2	non_synonymous	S543*	5	167553768	C	M
032	ODZ2	non_synonymous	S1760A	5	167673813	T	K
175	OGN	non_synonymous	I142K	9	95155370	A	W
323	OGT	non_synonymous	F878L	X	70787392	T	Y
323	OMG	non_synonymous	M104K	17	29623039	A	W
091	OPCML	non_synonymous	H9Y	11	131240726	C	Y
172	OPN1MW2	non_synonymous	R268H	X	153496075	G	R
642	OPRM1	non_synonymous	R431C	6	154412548	C	Y
618	OR10AG1	non_synonymous	V115M	11	55735597	C	Y
006	OR10C1	non_synonymous	V115M	6	29385399	G	R
032	OR10G9	non_synonymous	V221I	11	123894380	G	R
642	OR10K2	non_synonymous	M288I	1	158389793	C	M
145	OR11H4	non_synonymous	C207R	14	20711569	T	Y
157	OR2A12	non_synonymous	V60D	7	143792379	T	W
321	OR2M2	non_synonymous	I105M	1	248343602	A	R
063	OR2M4	frameshift	T76fs	1	248402457	*	-CA
182	OR2M4	non_synonymous	I74F	1	248402450	A	W
785	OR4C15	non_synonymous	P36L	11	55321889	C	Y
044	OR4C6	non_synonymous	R231W	11	55433333	C	Y
178	OR4K1	non_synonymous	V103I	14	20404132	G	R
030	OR4N2	non_synonymous	R122C	14	20295971	C	Y
172	OR4X1	non_synonymous	V143M	11	48285839	G	R
166	OR51M1	non_synonymous	C201S	11	5411230	G	S
273	OR52K1	non_synonymous	T136M	11	4510537	C	Y
159	OR56A1	non_synonymous	F114Y	11	6048594	A	W
039	OR5AU1	non_synonymous	R323H	14	21623217	C	Y
019	OR5AZ1P	non_synonymous	V188I	11	57685141	C	Y
274	OR5B21	non_synonymous	V196M	11	58274993	C	Y
178	OR5J2	non_synonymous	A173G	11	55944611	C	S
758	OR6T1	non_synonymous	R54C	11	123814386	G	R
020	OR7D2	non_synonymous	G152S	19	9296911	G	R
326	OR7G2	non_synonymous	T286S	19	9213127	T	W
022	OR8D2	non_synonymous	K298N	11	124189200	T	W
279	OSBPL1A	non_synonymous	F248L	18	21897353	A	W
159	OTUD1	non_synonymous	P379S	10	23729521	C	T
193	OXA1L	non_synonymous	H252L	14	23239135	A	W
052	P2RY8	non_synonymous	L220Q	X	1584793	A	W

290	PADI1	non_synonymous	R58S	1	17548864	C	M
282	PAK7	non_synonymous	S243R	20	9561053	G	K
007	PAPLN	non_synonymous	D933E	14	73730428	C	S
040	PAPSS2	splicing-site	-	10	89473069	T	W
758	PARP15	non_synonymous	I223S	3	122332012	T	K
175	PARVA	non_synonymous	K323T	11	12539257	A	M
082	PCDH11X	non_synonymous	Y919H	X	91133994	T	Y
165	PCDH11X	splicing-site	-	X	91518144	T	K
323	PCDH15	non_synonymous	M269I	10	56077115	C	Y
013	PCDH18	non_synonymous	M4I	4	138453231	C	M
275	PCDH24	non_synonymous	V1175M	5	176017672	G	R
044	PCDHA13	non_synonymous	D376Y	5	140262979	G	K
178	PCDHA2	non_synonymous	V441M	5	140175870	G	R
006	PCDHA9	non_synonymous	L409M	5	140229305	C	M
091	PCDHB13	non_synonymous	A361V	5	140594777	C	Y
091	PCDHGC5	non_synonymous	A91T	5	140793013	G	R
168	PCDHGC5	non_synonymous	N169K	5	140724107	C	M
041	PCLO	non_synonymous	E5018G	7	82390764	T	Y
165	PCLO	frameshift	T1689fs	7	82585203	*	+T
175	PCLO	non_synonymous	L1107F	7	82595783	T	W
280	PCLO	non_synonymous	L473R	7	82784539	A	M
189	PCMTD2	splicing-site	-	20	62899320	G	S
157	PCSK5	non_synonymous	R111Q	9	78601082	G	R
188	PCSK5	non_synonymous	R215H	9	78682882	G	R
642	PDE1C	non_synonymous	T481P	7	31867930	T	K
144	PDZRN3	non_synonymous	S790C	3	73433349	T	W
044	PENK	non_synonymous	R229W	8	57353950	G	R
785	PEX10	non_synonymous	V74I	1	2340271	C	T
761	PEX12	non_synonymous	K42N	17	33904915	C	S
019	PHC2	non_synonymous	Q119K	1	33836674	G	K
266	PHC2	splicing-site	-	1	33794611	C	S
100	PHF1	non_synonymous	C110*	6	33380563	T	W
039	PHGDH	splicing-site	-	1	120279735	A	G
155	PKD1L1	non_synonymous	P183S	7	47970891	G	R
049	PKD1L3	non_synonymous	A103T	16	72032282	C	Y
188	PKHD1	non_synonymous	R3620C	6	51524066	G	R
618	PLA2G4F	non_synonymous	T354A	15	42439966	T	Y
064	PLAT	non_synonymous	V66M	8	42046509	C	Y
264	PLCB1	non_synonymous	R101C	20	8608995	C	Y
193	PLCG1	non_synonymous	E289G	20	39792094	A	R
155	PLEC1	splicing-site	-	8	145001576	T	M
145	PLEKHA5	non_synonymous	D964N	12	19501339	G	R
280	PLEKHH1	non_synonymous	R344C	14	68029378	C	Y
375	PNOC	non_synonymous	L13V	8	28186711	C	S
325	PNPLA7	non_synonymous	R426T	9	140400484	C	S
328	PNPLA7	non_synonymous	E216*	9	140437114	C	M
064	PODNL1	splicing-site	-	19	14047274	G	S
040	POF1B	frameshift	Q197fs	X	84600999	*	-G
124	POF1B	non_synonymous	I546T	X	84558424	A	G
007	POLA1	non_synonymous	M962L	X	24767029	A	W

194	POLR2E	splicing-site	-	19	1090905	T	M
642	POM121L2	non_synonymous	P495T	6	27278467	G	K
188	POSTN	non_synonymous	G543E	13	38154030	C	Y
006	POT1	non_synonymous	Y223C	7	124499045	T	Y
013	POT1	non_synonymous	Y36N	7	124532338	A	W
044	POT1	splicing-site	-	7	124537268	A	W
157	POT1	non_synonymous	Y66*	7	124511022	A	M
184	POT1	non_synonymous	M1L	7	124537227	T	W
083	POTEH	non_synonymous	C139Y	22	16287470	C	Y
274	POU3F3	non_synonymous	K430*	2	105473256	A	W
013	POU3F4	non_synonymous	R279C	X	82764167	C	Y
328	PPAN-P2RY11	non_synonymous	V486D	19	10224486	T	W
145	PPFIA2	non_synonymous	R815W	12	81693139	G	R
186	PPM1D	non_synonymous	W154R	17	58678235	T	W
680	PPP1R3A	non_synonymous	L445I	7	113519868	G	K
321	PQLC2	splicing-site	-	1	19655065	G	S
186	PRAME	non_synonymous	W244*	22	22892370	C	Y
761	PRDM2	non_synonymous	V1168M	1	14107792	G	R
170	PRDM6	non_synonymous	G540R	5	122515962	G	R
020	PRDM9	non_synonymous	Y276F	5	23522939	A	W
100	PRDM9	non_synonymous	G307E	5	23523437	G	R
016	PRG4	non_synonymous	T901A	1	186277552	A	R
145	PRKD1	non_synonymous	A717D	14	30068249	G	K
175	PRKG1	non_synonymous	I684T	10	54053650	T	Y
029	PRLR	non_synonymous	R427K	5	35065780	C	Y
159	PRLR	non_synonymous	F501V	5	35065559	A	M
181	PROK2	non_synonymous	R122Q	3	71821900	C	Y
052	PROM1	non_synonymous	A772P	4	15985945	C	S
191	PROM1	non_synonymous	A766S	4	15985963	C	M
189	PROSC	non_synonymous	S46N	8	37623081	G	R
019	PROX1	non_synonymous	K611N	1	214178615	G	K
197	PRPF19	non_synonymous	T287P	11	60666746	T	K
018	PRRG3	splicing-site	-	X	150867295	T	K
152	PRUNE2	non_synonymous	A2922G	9	79253180	G	S
324	PSMD3	non_synonymous	L160V	17	38142894	C	S
029	PTDSS2	non_synonymous	R151W	11	486954	C	Y
194	PTGER2	non_synonymous	W313*	14	52794034	G	R
009	PTH2	splicing-site	-	19	49926467	T	M
063	PTK2	non_synonymous	D421E	8	141779690	A	W
090	PTK7	non_synonymous	R56Q	6	43096778	G	R
191	PTPN11	non_synonymous	A72V	12	112888199	C	Y
030	PTPN13	non_synonymous	L514R	4	87643520	T	K
170	PTPRB	non_synonymous	R1638K	12	70949730	C	Y
181	PTPRB	non_synonymous	R1895W	12	70933620	G	R
758	PTPRM	non_synonymous	D1436N	18	8406107	G	R
282	PTPRR	non_synonymous	R77H	12	71286586	C	Y
194	PZP	non_synonymous	W864L	12	9316752	C	M
184	QSER1	non_synonymous	Q161*	11	32953672	C	Y
321	RAB32	non_synonymous	T215N	6	146875707	C	M
054	RAB33A	non_synonymous	S181L	X	129318542	C	Y



184	RAB5A	non_synonymous	D53G	3	19992372	A	R
173	RAG1	non_synonymous	R759C	11	36597129	C	Y
165	RAI1	frameshift	Q280fs	17	17697101	*	-G
159	RALGPS2	non_synonymous	I266V	1	178848087	A	R
117	RANBP17	non_synonymous	T643M	5	170610233	C	Y
048	RANBP3L	non_synonymous	L189S	5	36262059	A	R
758	RANBP9	non_synonymous	S548L	6	13638070	G	R
275	RAP1GDS1	non_synonymous	L299V	4	99338024	T	K
091	RAP2C	non_synonymous	V153M	X	131348291	C	Y
082	RAPH1	non_synonymous	M428I	2	204322283	C	M
100	RASAL1	splicing-site	-	12	113565615	T	M
323	RASAL2	non_synonymous	G1039R	1	178427542	G	R
029	RASEF	non_synonymous	L177I	9	85670501	G	K
040	RASL11A	non_synonymous	R125*	13	27847275	C	Y
053	RBM18	non_synonymous	P26L	9	125023661	G	R
124	RBMX	non_synonymous	P167A	X	135958704	G	S
785	RDBP	frameshift	R219del4	6	31922440	*	-GTCTCGATCCCG
280	RDH16	non_synonymous	A237T	12	57346638	C	Y
027	REG1A	non_synonymous	C36R	2	79348729	T	Y
182	REG1B	non_synonymous	H103Q	2	79313505	A	M
006	RELN	non_synonymous	D368N	7	103338341	C	Y
172	RELN	non_synonymous	F1606I	7	103206791	A	W
189	REST	non_synonymous	Y223*	4	57777473	C	M
022	RFTN1	non_synonymous	G229E	3	16419365	C	Y
172	RFTN1	non_synonymous	S255R	3	16419286	G	S
030	RGS22	non_synonymous	P446L	8	101075659	G	R
023	RHCG	splicing-site	-	15	90015940	T	M
043	RHPN2	non_synonymous	H357L	19	33493188	T	W
054	RICTOR	non_synonymous	T1688I	5	38942996	G	R
032	RIF1	non_synonymous	I1511T	2	152320566	T	Y
018	RIMBP2	non_synonymous	D723A	12	130919313	T	K
006	RIMS2	non_synonymous	P889T	8	105025773	C	M
175	RIMS2	non_synonymous	S982G	8	105257236	A	R
186	RIMS2	non_synonymous	D1127V	8	105263861	A	W
785	RIOK1	non_synonymous	H348L	6	7405201	A	W
007	RIPK4	non_synonymous	W300G	21	43166266	A	M
322	RND3	non_synonymous	T155M	2	151328160	G	R
005	RNF103	non_synonymous	G61E	2	86849828	C	Y
680	RNF103	non_synonymous	P496S	2	86831538	G	R
280	RNF113A	non_synonymous	R291H	X	119004705	C	Y
090	RNF160	non_synonymous	G9W	21	30365240	C	M
051	RNF217	non_synonymous	R185H	6	125397951	G	R
184	RNF32	non_synonymous	E292K	7	156469010	G	R
008	RNPC3	non_synonymous	A70S	1	104070332	G	K
264	ROBO1	non_synonymous	V146F	3	78987814	C	M
044	ROBO2	non_synonymous	Q569K	3	77614127	C	M
280	ROR2	non_synonymous	D51E	9	94538045	G	K
189	ROS1	non_synonymous	Y1712S	6	117658448	T	K
193	ROS1	non_synonymous	L933R	6	117687253	A	M
264	RP1	non_synonymous	S1975I	8	55542366	G	K

022	RP11-88G17.1	non_synonymous	V170L	9	133057173	G	K
141	RP1L1	non_synonymous	Q2017H	8	10465557	C	M
275	RP4-788L13.1	non_synonymous	R431T	1	99771566	G	S
159	RPS13P2	non_synonymous	R99G	11	17097027	G	S
270	RPS15P5	non_synonymous	G129V	19	1440409	G	K
758	RPS6KB2	non_synonymous	S356G	11	67201866	A	R
006	RRBP1	non_synonymous	A688V	20	17622563	G	R
276	RREB1	non_synonymous	P1555L	6	7247347	C	Y
328	RRP7A	non_synonymous	N65S	22	42914033	T	C
172	RSPO2	non_synonymous	R28C	8	109094785	G	R
197	RSPRY1	non_synonymous	I522V	16	57269070	A	R
322	RSU1	non_synonymous	N16D	10	16859035	T	Y
049	RTCD1	non_synonymous	S67F	1	100733722	C	Y
319	RTTN	non_synonymous	A607P	18	67833408	C	S
321	RTTN	non_synonymous	Q1538*	18	67741183	G	R
090	RYR2	non_synonymous	A1488V	1	237758830	C	Y
194	RYR2	non_synonymous	R2125L	1	237791320	G	K
039	RYR3	non_synonymous	F3739L	15	34118922	C	M
328	RYR3	non_synonymous	R895L	15	33922145	G	K
032	SAG	non_synonymous	A352T	2	234250924	G	R
173	SAMD9L	non_synonymous	R828*	7	92762803	G	R
189	SCAMP5	non_synonymous	P83L	15	75309045	C	Y
282	SCCPDH	splicing-site	-	1	246923471	A	W
761	SCLY	non_synonymous	A223T	2	238990716	G	R
064	SCN2A	non_synonymous	E1373D	2	166231341	G	K
194	SCN2B	non_synonymous	R137H	11	118038838	C	T
017	SCN3B	non_synonymous	L10P	11	123524481	A	R
124	SCN4A	non_synonymous	K1341*	17	62020453	T	W
030	SCN5A	non_synonymous	R1512W	3	38597155	G	R
270	SCN8A	non_synonymous	V755A	12	52145271	T	Y
172	SEC14L2	non_synonymous	H280N	22	30812003	C	M
044	SECISBP2	non_synonymous	K15R	9	91934574	A	R
155	SEMA3C	non_synonymous	E238K	7	80434955	C	Y
005	SENP2	splicing-site	-	3	185337291	G	R
023	SERPINA7	non_synonymous	S373L	X	105277621	G	A
054	SETD1A	non_synonymous	Y370C	16	30976172	A	R
006	SF3B1	non_synonymous	N626Y	2	198267481	T	W
009	SF3B1	non_synonymous	K700E	2	198266834	T	Y
019	SF3B1	non_synonymous	V701F	2	198266831	C	M
029	SF3B1	non_synonymous	K700E	2	198266834	T	Y
053	SF3B1	non_synonymous	T663I	2	198267369	G	R
083	SF3B1	non_synonymous	D894G	2	198265476	T	Y
156	SF3B1	non_synonymous	K700E	2	198266834	T	Y
182	SF3B1	non_synonymous	N626Y	2	198267481	T	W
197	SF3B1	non_synonymous	G742D	2	198266611	C	Y
758	SF3B1	non_synonymous	K700E	2	198266834	T	Y
100	SFRS1	frameshift	G4fs	17	56084489	*	-T
274	SFRS1	non_synonymous	Y82*	17	56083837	G	S
282	SFRS7	non_synonymous	L18Q	2	38977312	A	W
321	SGCG	frameshift	S84fs	13	23808805	*	-AG

174	SGIP1	non_synonymous	G575D	1	67184977	G	R
322	SH3RF2	non_synonymous	R201*	5	145379843	C	T
016	SHANK1	frameshift	S638ins	19	51200870	*	+AGC
016	SHPRH	non_synonymous	M710V	6	146264389	T	Y
006	SI	non_synonymous	R91T	3	164786967	C	S
043	SI	non_synonymous	T1680I	3	164709210	G	R
048	SI	non_synonymous	W1493C	3	164716389	C	M
100	SI	non_synonymous	D1193N	3	164735605	C	Y
043	SIK2	non_synonymous	I595T	11	111591626	T	Y
146	SIRT4	non_synonymous	R156C	12	120741830	C	Y
019	SKAP2	non_synonymous	V240I	7	26765125	C	Y
322	SKIV2L2	non_synonymous	R200H	5	54635921	G	R
193	SLA	splicing-site	-	8	134060179	G	S
680	SLC12A4	non_synonymous	L158F	16	67991818	G	R
117	SLC12A5	splicing-site	-	20	44664415	G	A
083	SLC16A2	non_synonymous	C283Y	X	73744244	G	R
325	SLC1A3	non_synonymous	I465T	5	36684070	T	Y
375	SLC24A5	non_synonymous	I181V	15	48427132	A	R
184	SLC38A6	non_synonymous	L418H	14	61518816	T	W
049	SLC44A4	non_synonymous	P403L	6	31836957	G	A
188	SLC45A1	non_synonymous	R301*	1	8390352	C	Y
029	SLC47A1	non_synonymous	R333Q	17	19463577	G	R
039	SLC4A10	non_synonymous	S615C	2	162762244	C	S
197	SLC4A10	non_synonymous	Q220E	2	162719464	C	S
280	SLC4A10	non_synonymous	R799L	2	162807213	G	K
181	SLC4A8	non_synonymous	N1068D	12	51890948	A	R
090	SLC6A5	non_synonymous	S410A	11	20639398	T	K
680	SLC7A3	non_synonymous	R600H	X	70145724	C	Y
375	SLC7A6	non_synonymous	R348Q	16	68328628	G	R
680	SLC9A11	non_synonymous	L84H	1	173567149	A	W
016	SLCO1B1	non_synonymous	P484H	12	21358921	C	M
642	SLCO1B1	non_synonymous	I97T	12	21327574	T	Y
019	SLITRK3	non_synonymous	E813K	3	164906182	C	Y
181	SLITRK6	non_synonymous	L12P	13	86370609	A	R
090	SMARCD3	non_synonymous	D351N	7	150937320	C	Y
045	SNAP91	frameshift	E224fs	6	84350910	*	+A
185	SNTG2	non_synonymous	D174H	2	1168798	G	S
049	SNX13	non_synonymous	N723S	7	17854497	T	Y
018	SNX7	non_synonymous	T232P	1	99161128	A	M
090	SP140	non_synonymous	R380P	2	231134655	G	S
083	SPA17	non_synonymous	V116A	11	124564233	T	Y
170	SPAG17	non_synonymous	R1641S	1	118539123	C	M
048	SPAG4L	non_synonymous	E178G	20	31583426	T	Y
264	SPC24	non_synonymous	R106G	19	11258783	T	Y
043	SPHKAP	non_synonymous	A930T	2	228882782	C	Y
323	SPHKAP	non_synonymous	Q986*	2	228882614	G	R
159	SPRR1B	non_synonymous	P43A	1	153004948	C	S
278	SPRY3	non_synonymous	P34L	X	155003634	C	Y
280	SPRY3	non_synonymous	M225I	X	155004208	G	R
276	SPTBN1	non_synonymous	R681W	2	54856312	C	Y

186	SRFBP1	non_synonymous	S303L	5	121356338	C	Y
110	SRRT	non_synonymous	G135D	7	100479679	G	R
090	SSPO	non_synonymous	A4542T	7	149521545	G	R
159	ST6GALNAC1	non_synonymous	T179M	17	74625389	G	R
019	STARD9	non_synonymous	M2280L	15	42980872	A	W
188	STAT6	splicing-site	-	12	57496281	A	G
197	STK36	non_synonymous	L1147V	2	219563706	C	S
172	STOX2	non_synonymous	I697K	4	184932081	T	W
290	SULT1C2	non_synonymous	S132P	2	108917368	T	Y
194	SULT2A1	non_synonymous	V236A	19	48377952	A	R
194	SUSD4	non_synonymous	T290P	1	223402593	T	K
043	SVIL	non_synonymous	E147K	10	29839914	C	Y
618	SWAP70	frameshift	L207fs	11	9746411	*	+A
040	SYN3	non_synonymous	V146M	22	33327400	C	Y
642	SYNC	non_synonymous	D338H	1	33160687	C	S
272	SYNE1	non_synonymous	M4357I	6	152652749	C	M
063	SYNPO2	non_synonymous	T601S	4	119951732	C	S
124	SYT17	non_synonymous	R28W	16	19184800	C	Y
016	TAAR6	non_synonymous	K258N	6	132892234	A	M
052	TADA3L	non_synonymous	Q266*	3	9828704	G	R
141	TAF2	non_synonymous	L994M	8	120759073	A	W
178	TAF4B	non_synonymous	K288M	18	23854998	A	W
175	TAL1	non_synonymous	A159D	1	47689747	G	K
040	TAS2R16	non_synonymous	H209Y	7	122635064	G	R
181	TBC1D12	non_synonymous	R431*	10	96253201	C	Y
181	TBC1D16	non_synonymous	R482C	17	77922768	G	R
270	TBC1D8	non_synonymous	H759P	2	101644841	T	K
157	TBPL1	non_synonymous	S73R	6	134303787	A	M
175	TCF7L1	non_synonymous	M292T	2	85532412	T	Y
124	TCF7L2	non_synonymous	R119Q	10	114920413	G	R
174	TCL1A	splicing-site	-	14	96180283	G	Y
039	TDRD1	non_synonymous	N65K	10	115947785	C	M
124	TDRD6	non_synonymous	K1519N	6	46660422	A	W
009	TDRD9	non_synonymous	E258K	14	104436884	G	R
013	TEAD2	frameshift	P144fs	19	49858606	*	-GC
017	TECTA	non_synonymous	N886S	11	121000636	A	R
264	TEKT2	non_synonymous	E48K	1	36550664	G	R
266	TET1	non_synonymous	P307H	10	70333015	C	M
188	TET2	non_synonymous	S1563F	4	106196355	C	Y
152	TET3	non_synonymous	R443H	2	74274651	G	R
156	TFEB	non_synonymous	N327S	6	41655496	T	Y
082	TGFBR3	non_synonymous	R564*	1	92182142	G	R
082	TGIF2LX	non_synonymous	E204*	X	89177694	G	K
117	THNSL1	non_synonymous	V480I	10	25313590	G	R
091	TIE1	non_synonymous	V765M	1	43779523	G	R
785	TIMD4	non_synonymous	G374D	5	156346484	C	Y
191	TINAG	non_synonymous	R191L	6	54191662	G	K
045	TLR2	non_synonymous	D327V	4	154625039	A	W
280	TLR2	non_synonymous	D327V	4	154625039	A	W
042	TLR5	non_synonymous	N96K	1	223286086	G	K

280	TLR6	non_synonymous	P403S	4	38829888	G	R
064	TMC2	non_synonymous	N434S	20	2582835	A	R
275	TMCO5B	non_synonymous	T248I	15	33528132	G	R
032	TMEM106C	non_synonymous	P108L	12	48359692	C	Y
044	TMEM131	non_synonymous	S1256C	2	98409226	G	S
189	TMEM132A	non_synonymous	V798G	11	60703697	T	G
159	TMEM132D	non_synonymous	V304M	12	130184413	C	Y
006	TMEM194A	non_synonymous	S152N	12	57464474	C	Y
141	TMEM63B	non_synonymous	G783R	6	44122468	G	R
192	TMEM87B	non_synonymous	I466V	2	112858218	A	R
290	TMPRSS11D	non_synonymous	R6G	4	68725389	G	S
324	TMPRSS12	non_synonymous	I304F	12	51281159	A	W
264	TMTC2	non_synonymous	K378E	12	83290074	A	R
785	TMTC2	non_synonymous	E765G	12	83455573	A	R
083	TNFSF15	non_synonymous	E164D	9	117552996	T	W
324	TNIK	non_synonymous	F1046L	3	170801977	A	R
280	TOMM40	non_synonymous	V190G	19	45397249	T	K
159	TOPBP1	non_synonymous	G202R	3	133374272	C	S
178	TOR1A	non_synonymous	M204T	9	132581129	A	R
618	TP53	splicing-site	-	17	7576851	T	G
155	TPCN1	non_synonymous	V586M	12	113724805	G	R
007	TPSAB1	non_synonymous	G30V	16	1291160	G	K
274	TPTTE	non_synonymous	R507W	21	10908826	T	W
082	TRAF1	non_synonymous	N379S	9	123667413	T	Y
042	TRAPPC9	non_synonymous	G122V	8	141461402	C	M
019	TRHR	non_synonymous	F363Y	8	110131575	T	W
146	TRIM29	non_synonymous	F194I	11	120008160	A	W
264	TRIM46	non_synonymous	E368D	1	155150672	A	T
321	TRIM55	non_synonymous	A437V	8	67066355	C	Y
185	TRIM64C	non_synonymous	V366A	11	49075513	A	R
618	TRIML1	non_synonymous	M7L	4	189060731	A	M
618	TRIO	non_synonymous	R1982H	5	14472733	G	R
324	TRIOBP	non_synonymous	R679Q	22	38120599	G	R
270	TRMU	non_synonymous	D172H	22	46746223	G	S
040	TRO	frameshift	V878fs	X	54955790	*	-C
040	TRO	frameshift	F879del2	X	54955792	*	-TCAGCA
197	TRO	non_synonymous	L1113F	X	54956494	C	Y
174	TRPA1	non_synonymous	Q1000K	8	72938248	G	K
178	TRPC4	non_synonymous	R699S	13	38213434	C	S
041	TRPM1	non_synonymous	A165P	15	31359325	C	S
188	TTC7B	splicing-site	-	14	91077185	A	W
264	TTC9B	non_synonymous	A188T	19	40723142	C	Y
155	TTLL9	splicing-site	-	20	30496392	A	M
170	TTN	non_synonymous	H28851R	2	179411996	T	Y
170	TTN	non_synonymous	R12194*	2	179494168	G	R
274	TTN	non_synonymous	T2963P	2	179634421	T	K
758	TUBA1	non_synonymous	V181M	2	220115880	C	Y
192	TUBA3C	non_synonymous	F138L	13	19751711	A	R
274	TUBGCP6	non_synonymous	K1635T	22	50656967	T	K
328	TXNDC3	non_synonymous	T240S	7	37907400	A	W

016	U2AF2	non_synonymous	Q190L	19	56173950	A	W
275	U2AF2	non_synonymous	Q143L	19	56172497	A	W
172	UBE2Q1	non_synonymous	V136G	1	154528361	A	M
272	UGCGL1	non_synonymous	Q1462*	2	128944281	C	Y
044	UGT2B4	non_synonymous	I331V	4	70355168	T	Y
267	UGT8	non_synonymous	R187C	4	115544595	C	Y
029	UMODL1	non_synonymous	N266S	21	43510414	A	R
032	UNC13C	non_synonymous	R1343*	15	54590047	C	Y
189	UNC13C	non_synonymous	D923E	15	54307869	T	W
041	UNC5D	non_synonymous	V319I	8	35544098	G	R
324	UNC5D	non_synonymous	A724V	8	35608320	C	Y
019	UNQ9391	non_synonymous	A151T	8	10388908	G	R
053	UPP2	splicing-site	-	2	158971611	A	W
040	URM1	frameshift	G13del5	9	131140316	*	-GTGGTGC GGAGCTCC
039	USH2A	non_synonymous	N1596H	1	216262454	T	K
157	USH2A	non_synonymous	T2310M	1	216143995	G	R
013	USP13	non_synonymous	S356N	3	179439356	G	R
064	USP49	non_synonymous	P476S	6	41771679	G	R
323	USP53	non_synonymous	R580Q	4	120192754	G	R
082	USP9X	non_synonymous	M1916V	X	41075566	A	R
188	VCAN	non_synonymous	G838E	5	82816638	G	R
189	VDR	non_synonymous	R402P	12	48238608	C	S
022	VIL2	non_synonymous	T25A	6	159210343	T	Y
156	VILL	splicing-site	-	3	38043086	T	K
194	VILL	non_synonymous	S618P	3	38045792	T	Y
325	VIPR2	non_synonymous	R98W	7	158889543	G	R
189	VIT	splicing-site	-	2	37036130	T	G
022	VOPP1	splicing-site	-	7	55605250	T	M
193	VPRBP	non_synonymous	D1005G	3	51457410	T	Y
290	VPRBP	non_synonymous	I77L	3	51500851	T	K
110	VSTM2A	non_synonymous	M165R	7	54617723	T	K
159	VSTM2L	non_synonymous	G66S	20	36560111	G	R
145	VWA2	frameshift	R676ins3	10	116049152	*	+GGAGGCTTG
032	VWA3A	non_synonymous	R1134C	16	22163878	C	Y
041	VWA3B	splicing-site	-	2	98804436	A	W
280	WAS	splicing-site	-	X	48546844	T	G
264	WBP1	non_synonymous	T144A	2	74687155	A	R
174	WDFY4	non_synonymous	V400I	10	49939223	G	R
020	WDR24	non_synonymous	R371H	16	737354	C	Y
194	WDR24	splicing-site	-	16	737825	T	M
016	WDR40C	non_synonymous	W196L	X	125299321	C	A
280	WDR42B	non_synonymous	N272I	X	27998637	T	W
194	WDR45	non_synonymous	H60P	X	48932381	T	K
272	WDR59	non_synonymous	K630R	16	74927688	T	Y
761	WDR63	non_synonymous	L380I	1	85560203	C	M
785	WFIKKN2	non_synonymous	V82I	17	48916893	G	R
324	WFS1	non_synonymous	P885S	4	6304175	C	Y
009	WNT2	non_synonymous	D226N	7	116937843	C	Y
758	WRNIP1	splicing-site	-	6	2769118	T	W
178	XIRP2	non_synonymous	L557M	2	168099571	C	M

053	XPO1	non_synonymous	E571K	2	61719472	C	Y
270	XPO1	non_synonymous	E571V	2	61719471	T	W
197	XPOT	non_synonymous	I848N	12	64828377	T	W
032	YLPM1	non_synonymous	S660L	14	75248725	C	Y
117	YTHDF3	non_synonymous	T559I	8	64100239	C	Y
173	YY1AP1	non_synonymous	H131Q	1	155657863	G	S
016	ZBTB38	non_synonymous	P643S	3	141163154	C	Y
276	ZBTB9	non_synonymous	K46T	6	33423014	A	M
051	ZC3H12C	non_synonymous	R611H	11	110035639	G	R
170	ZC3H13	non_synonymous	R840H	13	46544550	C	Y
018	ZEB1	non_synonymous	R181H	10	31799661	G	R
023	ZFHx4	non_synonymous	P3079S	8	77768440	C	Y
270	ZFP30	non_synonymous	H176Q	19	38126914	A	M
168	ZFPM2	non_synonymous	L632F	8	106814206	A	M
273	ZFYVE16	non_synonymous	N925D	5	79743893	A	R
267	ZHX1	non_synonymous	V206I	8	124267571	C	Y
264	ZMYM1	non_synonymous	P116R	1	35563095	C	S
016	ZMYM3	non_synonymous	L1142V	X	70463693	G	C
039	ZMYM3	non_synonymous	V850M	X	70466233	C	T
274	ZNF133	non_synonymous	K422T	20	18296718	A	M
326	ZNF205	non_synonymous	E452D	16	3170017	G	S
326	ZNF205	non_synonymous	C456S	16	3170027	T	W
159	ZNF28	non_synonymous	T643N	19	53303170	G	K
063	ZNF285B	non_synonymous	K61T	19	44892225	T	K
165	ZNF292	frameshift	L1011fs	6	87966379	*	-CA
041	ZNF324	non_synonymous	V8G	19	58980575	T	K
064	ZNF333	non_synonymous	K476N	19	14829567	G	K
030	ZNF337	non_synonymous	D116N	20	25657578	C	Y
043	ZNF343	non_synonymous	P548S	20	2463965	G	R
272	ZNF366	non_synonymous	L289P	5	71756458	A	R
043	ZNF383	non_synonymous	H332R	19	37734133	A	R
145	ZNF385A	non_synonymous	A256V	12	54764778	G	R
319	ZNF430	non_synonymous	V72A	19	21216380	T	Y
033	ZNF498	non_synonymous	E83V	7	99217477	A	W
185	ZNF507	non_synonymous	I14T	19	32843777	T	Y
030	ZNF530	non_synonymous	T458A	19	58118265	A	R
063	ZNF536	non_synonymous	N613I	19	30936307	A	W
178	ZNF572	non_synonymous	M31V	8	125988601	A	R
188	ZNF586	non_synonymous	P121S	19	58290316	C	Y
282	ZNF615	non_synonymous	R509C	19	52496837	G	R
276	ZNF667	non_synonymous	P95R	19	56973735	G	S
042	ZNF668	non_synonymous	V476G	16	31072822	A	M
270	ZNF676	non_synonymous	K311E	19	22363684	T	Y
758	ZNF711	non_synonymous	R284*	X	84520195	C	T
145	ZNF730	non_synonymous	H334R	19	23328847	A	R
022	ZNF81	non_synonymous	G270E	X	47774854	G	R
039	ZNF99	non_synonymous	S599L	19	22940642	G	R
270	ZNF99	non_synonymous	L959F	19	22939296	G	R
033	ZRSR2	splicing-site	-	X	15827321	A	R
040	ZW10	non_synonymous	G637E	11	113608400	C	Y

**Supplementary Table 6.** RM-CLL genes

Class 1										
Gene	Cases									
ADAM2	013	039								
ALS2CL	173	270								
ARHGAP28	013	110								
ASXL1	030	145	182							
ATM	006	020	048	145						
BRAF	148	279								
BRUNOL4	171	785								
C12orf64	006	322								
CD36	181	273								
CDH9	324	CLL2								
CHD2	007	043	175	181	185					
CNOT3	194	CLL1								
COL25A1	054	194								
CSMD3	043	117	168	279						
CYP2A7	033	CLL1								
DDX3X	188	328								
DPP6	266	323								
DTNA	013	170								
EGR2	082	290								
EPHB1	178	270								
FAM117A	185	324								
FGFR2	064	278								
FSTL5	264	280								
FUBP1	016	270								
GNAT1	136	282								
KCNAB1	032	273								
LPHN3	053	082	091							
LRP1B	005	274	276	322	326					
LUZP2	170	290								
MUC2	017	267	290	322						
MYD88	181	785	CLL3							
NLN	156	197								
NOTCH1	019	048	156	184	321					
NXF1	023	082	083							
OR2M4	063	182								
PCDHGC5	091	168								
PHC2	019	266								
POF1B	040	124								
POT1	006	013	044	157	184					
PRDM9	020	100								
PRLR	029	159								
PROM1	052	191								
RFTN1	022	172								
RIMS2	006	175	186							
RNF103	005	680								
SF3B1	006	009	019	029	053	083	156	182	197	758



SFRS1	100	274		
SI	006	043	048	100
SLC4A10	039	197	280	
SLCO1B1	016	642		
SNX7	018	CLL4		
SPRY3	278	280		
TLR2	045	280		
TMTC2	264	785		
TRO	040	197		
U2AF2	016	275		
UNC5D	041	324		
VILL	156	194		
WDR24	020	194		
XPO1	053	270		
<b>Class 2</b>				
<b>Gene</b>	<b>Cases</b>			
AKAP6	110	189		
C2orf21	141	172		
CDH23	008	192	761	
DOCK4	051	282		
FAT3	618	761		
HMCN1	124	195		
HYDIN	018	091	181	761
KIAA1632	032	155		
LPHN2	063	192		
PCDH11X	082	165		
PCLO	041	165	175	280
PNPLA7	325	328		
ROS1	189	193		
RTTN	319	321		
RYR2	090	194		
TP53	618			
UNC13C	032	189		
VPRBP	193	290		

Cases CLL1, CLL2, CLL3 and CLL4 have been described in Puente X.S. et al., *Nature* (2011), 475:101-5

**Supplementary Table 7.** Structural variants\* involving RM-CLL genes

<b>Sample</b>	<b>Chr</b>	<b>Start</b>	<b>End</b>	<b>Structural variant</b>	<b>RM-CLL genes involved</b>
016	1	158,895,935	207,100,978	Inversion	HMCN1
048	3	120,468,448	199,324,877	Gain	EPHB1, KCNAB1, SI
016	4	55,259,599	190,916,819	Gain	LPHN3, COL25A1, TLR2, FSTL5
016	6	92,406,400	117,192,979	Inversion	ROS1
064	8	59,529,447	144,292,596	Gain	RIMS2, CSMD3
026	11	78,834,995	115,325,262	Loss	FAT3, ATM
032	12			Gain (Trisomy)	SLCO1B1, C12orf64, TMTC2
064	12			Gain (Trisomy)	SLCO1B1, C12orf64, TMTC2
016	18	118,560	19,284,700	Loss	ARHGAP28
009	X	132,393,797	155,227,312	Gain	SPRY3

\*Structural variants were assessed by aCGH, paired-end mapping and depth of coverage in 10 cases analyzed by whole genome sequencing

**Supplementary Table 8.** Biochemical pathways with somatic mutations in CLL

KEGG pathways			
Term	Q-value	Genes	Cancer types
mRNA surveillance pathway	0.001	EIF4A3, MAGOH, MSI2, NCBP2, NUDT21, NXF1	
Bladder cancer	0.003	EGFR, IL8, MAP2K2, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Prostate cancer	0.003	CREB1, EGFR, FGFR2, MAP2K2, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Spliceosome	0.003	EIF4A3, MAGOH, NCBP2, RBMX, SF3B1, U2AF2	
RNA transport	0.021	EIF4A3, MAGOH, NCBP2, NXF1, XPO1	
Endometrial cancer	0.021	EGFR, MAP2K2, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal
Malaria	0.021	IL8, MYD88, TLR2	
Non-small cell lung cancer	0.021	EGFR, MAP2K2, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas
Toll-like receptor signaling pathway	0.021	IL8, MAP2K2, MYD88, TLR2	Breast, Lung
Pathways in cancer	0.025	EGFR, FGFR2, IL8, ITGA2B, MAP2K2, TP53, TRAF1	
Glioma	0.028	EGFR, MAP2K2, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Melanoma	0.033	EGFR, MAP2K2, TP53	Bladder, Breast, Colorectal, Gastric, HeadNeck, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Ribosome biogenesis in eukaryotes	0.043	NXF1, RRP7A, XPO1	
Small cell lung cancer	0.045	ITGA2B, TP53, TRAF1	Breast, Colorectal, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas
Gap junction	0.046	EGFR, MAP2K2, TUBA3C	Colorectal, Leukemia, Lung, Brain, Melanoma, Pancreas
Apoptosis	0.046	ATM, MYD88, TP53	Lung, Melanoma
Chagas disease	0.062	IL8, MYD88, TLR2	
Huntington's disease	0.065	CREB1, POLR2E, TBPL1, TP53	
Cell cycle	0.092	ATM, CCNA2, TP53	Colorectal, Leukemia, Lung, Melanoma
Regulation of actin cytoskeleton	0.094	EGFR, FGFR2, ITGA2B, MAP2K2	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma
Hepatitis C	0.095	EGFR, IL8, TP53	
GO Biological Processes			
Term	Q-value	Genes	Cancer types
termination of RNA polymerase II transcription	0.001	MAGOH, NCBP2, NUDT21, U2AF2	
lactation	0.001	BCAT2, CREB1, PRLR, VDR	

nuclear mRNA splicing, via spliceosome	0.001	MAGOH, NCBP2, NUDT21, POLR2E, RBMX, SF3B1, U2AF2	
RNA splicing	0.001	EIF4A3, MAGOH, NCBP2, NUDT21, POLR2E, RBMX, SF3B1, U2AF2	
mRNA 3'-end processing	0.001	MAGOH, NCBP2, NUDT21, U2AF2	
transcription from RNA polymerase II promoter	0.001	CREB1, FUBP1, MAGOH, NCBP2, NUDT21, POLR2E, TBPL1, U2AF2	Leukemia, Lung, Melanoma
Toll signaling pathway	0.003	CREB1, MAP2K2, MYD88, TLR2	
toll-like receptor 1 signaling pathway	0.003	CREB1, MAP2K2, MYD88, TLR2	
toll-like receptor signaling pathway	0.003	CREB1, MAP2K2, MYD88, TLR2	
gene expression	0.003	MAGOH, NCBP2, NUDT21, NXF1, POLR2E, RBMX, SF3B1, U2AF2, VDR	Leukemia, Melanoma
nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	0.003	EIF4A3, MAGOH, NCBP2	
mRNA export from nucleus	0.003	MAGOH, NCBP2, NXF1, U2AF2	Brain
MyD88-dependent toll-like receptor signaling pathway	0.003	CREB1, MAP2K2, MYD88, TLR2	
positive regulation of nitric oxide biosynthetic process	0.003	DDAH1, EGFR, TLR2	
toll-like receptor 2 signaling pathway	0.003	CREB1, MAP2K2, MYD88, TLR2	
toll-like receptor 4 signaling pathway	0.003	CREB1, MAP2K2, MYD88, TLR2	
positive regulation of gene-specific transcription from RNA polymerase II promoter	0.005	CREB1, FGFR2, TAL1, TLR2, TP53	
interspecies interaction between organisms	0.006	CREB1, DDX3X, KCTD5, NXF1, POLR2E, TP53, XPO1	
mRNA transport	0.008	EIF4A3, NXF1, XPO1	

response to DNA damage stimulus	0.013	ATM, C9orf80, MGMT, TP53	Brain, Leukemia, Lung, Melanoma
Ras protein signal transduction	0.016	CCNA2, MAP2K2, TP53	Bladder, Brain, Breast, Colorectal, Gastric, Leukemia, Lung, Melanoma
mRNA processing	0.022	EIF4A3, MBNL2, NCBP2, NUDT21, U2AF2	
transcription	0.022	MAGOH, NCBP2, NUDT21, POLR2E, U2AF2	Leukemia, Lung, Melanoma, Sarcoma
positive regulation of NF-kappaB transcription factor activity	0.022	MYD88, TLR2, TRAF1	Lung, Melanoma
regulation of apoptosis	0.048	CASP1, CREB1, TP53, TRAF1	Leukemia, Lung, Lymphoma, Melanoma
regulation of cell proliferation	0.051	EGFR, MYD88, PTGER2	Bladder, Brain, Colorectal, Gastric, Leukemia, Lung, Lymphoma, Melanoma, Renal
cell cycle arrest	0.06	ATM, IL8, TP53	Leukemia, Lung, Melanoma
positive regulation of I-kappaB kinase/NF-kappaB cascade	0.068	CASP1, MYD88, TRAF1	
cell death	0.068	ATM, CASP1, DPP6	Colorectal, Leukemia, Lung, Lymphoma, Melanoma
signal transduction	0.068	ATM, CASP1, CREB1, EGFR, IL8, MYD88, PENK, RAB33A, RAP2C, TLR2, TRAF1, VDR, VOPP1	Brain, Colorectal, Gastric, Leukemia, Lung, Lymphoma, Melanoma, Ovary
innate immune response	0.078	CREB1, MAP2K2, MYD88, TLR2	
negative regulation of gene-specific transcription from RNA polymerase II promoter	0.088	FGFR2, TP53, VDR	
<b>NCI Nature Pathways</b>			
<b>Term</b>	<b>Q-value</b>	<b>Genes</b>	<b>Cancer types</b>
p75(NTR)-mediated signaling	0.011	MAGEH1, MYD88, TP53	
AP-1 transcription factor network	0.011	CREB1, IL8, PENK, TP53	
Glucocorticoid receptor regulatory network	0.011	CREB1, CSN2, IL8, TP53	
Validated transcriptional targets of deltaNp63 isoforms	0.023	ADA, ATM, VDR	
ATF-2 transcription factor network	0.023	CCNA2, CREB1, IL8	

Validated transcriptional targets of TAp63 isoforms	0.023	ADA, EGR2, VDR
Direct p53 effectors	0.034	CASP1, EGFR, TP53, VDR

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**Supplementary Table 9.** Pathway analysis of the genes found mutated in *IGHV*-mutated CLL

KEGG pathways			
Term	Q-value	Genes	Cancer types
Bladder cancer	0.006	EGFR, IL8, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Malaria	0.006	IL8, MYD88, TLR2	
mRNA surveillance pathway	0.014	EIF4A3, MSI2, NUDT21	
Prostate cancer	0.014	EGFR, FGFR2, TP53	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Chagas disease	0.015	IL8, MYD88, TLR2	
Toll-like receptor signaling pathway	0.015	IL8, MYD88, TLR2	Breast, Lung
Spliceosome	0.022	EIF4A3, RBMX, SF3B1	
Hepatitis C	0.023	EGFR, IL8, TP53	
Pathways in cancer	0.048	EGFR, FGFR2, IL8, TP53	
Endocytosis	0.052	CHMP2B, EGFR, FGFR2	
Cytokine-cytokine receptor interaction	0.085	EGFR, IL8, PRLR	Gastric
MAPK signaling pathway	0.085	EGFR, FGFR2, TP53	Breast, Colorectal, Leukemia, Lung, Melanoma
GO Biological Processes			
Term	Q-value	Genes	Cancer types
lactation	0.003	BCAT2, PRLR, VDR	
RNA splicing	0.007	EIF4A3, NUDT21, POLR2E, RBMX, SF3B1	
nuclear mRNA splicing, via spliceosome	0.007	NUDT21, POLR2E, RBMX, SF3B1	
positive regulation of gene-specific transcription from RNA polymerase II promoter	0.007	FGFR2, TAL1, TLR2, TP53	
regulation of cell proliferation	0.019	EGFR, MYD88, PTGER2	Bladder, Brain, Colorectal, Gastric, Leukemia, Lung, Lymphoma, Melanoma, Renal
response to DNA damage stimulus	0.02	C9orf80, MGMT, TP53	Brain, Leukemia, Lung, Melanoma
gene expression	0.026	NUDT21, POLR2E, RBMX, SF3B1, VDR	Leukemia, Melanoma
negative regulation of gene-specific transcription from RNA polymerase II promoter	0.027	FGFR2, TP53, VDR	
cell surface receptor linked signaling pathway	0.068	EGFR, MYD88, PRLR	Brain, Colorectal, Gastric, Leukemia, Lung, Melanoma
multicellular organismal development	0.1	CLC, PHC2, TAL1, TCL1A, TP53, VDR	Bladder, Brain, Colorectal, Gastric, HeadNeck, Leukemia, Lung, Melanoma
DNA repair	0.1	C9orf80, MGMT, POLR2E	Leukemia, Lung, Melanoma

**NCI Nature Pathways**

<b>Term</b>	<b>Q-value</b>	<b>Genes</b>	<b>Cancer types</b>
Direct p53 effectors	0.012	EGFR, TP53, VDR	



**Supplementary Table 10.** Pathway analysis of the genes found mutated in *IGHV*- unmutated CLL

KEGG pathways			
Term	Q-value	Genes	Cancer types
Prostate cancer	0.005	CREB1, EGFR, FGFR2, MAP2K2	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma, Ovary, Pancreas, Renal, Sarcoma
Spliceosome	0.01	MAGOH, NCBP2, SF3B1, U2AF2	
mRNA surveillance pathway	0.012	MAGOH, NCBP2, NXF1	
RNA transport	0.012	MAGOH, NCBP2, NXF1, XPO1	
Regulation of actin cytoskeleton	0.021	EGFR, FGFR2, ITGA2B, MAP2K2	Bladder, Breast, Colorectal, Gastric, Leukemia, Lung, Brain, Melanoma
Pathways in cancer	0.021	EGFR, FGFR2, ITGA2B, MAP2K2, TRAF1	
GO Biological Processes			
Term	Q-value	Genes	Cancer types
mRNA 3'-end processing	0.001	MAGOH, NCBP2, U2AF2	
termination of RNA polymerase II transcription	0.001	MAGOH, NCBP2, U2AF2	
transcription from RNA polymerase II promoter	0.001	CREB1, FUBP1, MAGOH, NCBP2, TBPL1, U2AF2	Leukemia, Lung, Melanoma
mRNA export from nucleus	0.001	MAGOH, NCBP2, NXF1, U2AF2	Brain
nuclear mRNA splicing, via spliceosome	0.003	MAGOH, NCBP2, SF3B1, U2AF2	
interspecies interaction between organisms	0.01	CREB1, DDX3X, KCTD5, NXF1, XPO1	
gene expression	0.024	MAGOH, NCBP2, NXF1, SF3B1, U2AF2	Leukemia, Melanoma
RNA splicing	0.024	MAGOH, NCBP2, SF3B1, U2AF2	
axon guidance	0.03	CREB1, EGFR, ITGA2B, MAP2K2	
regulation of apoptosis	0.042	CASP1, CREB1, TRAF1	Leukemia, Lung, Lymphoma, Melanoma
protein phosphorylation	0.047	ATM, CREB1, EGFR, FGFR2, MAP2K2	Brain, Breast, Colorectal, Gastric, Leukemia, Lung, Melanoma
transcription	0.051	MAGOH, NCBP2, U2AF2	Leukemia, Lung, Melanoma, Sarcoma
mRNA processing	0.051	MBNL2, NCBP2, U2AF2	
signal transduction	0.079	ATM, CASP1, CREB1, EGFR, PENK, RAB33A, TRAF1, VOPP1	Brain, Colorectal, Gastric, Leukemia, Lung, Lymphoma, Melanoma, Ovary

**Supplementary Table 11.** CLL non-synonymous somatic mutations in *SF3B1*

<b>Mutation</b>	<b>Exon</b>	<b>N</b>	<b>Frequency</b>
p.K700E	15	9	3.2%
p.G742D	16	6	2.2%
p.N626Y	14	2	0.7%
p.T663I	14	2	0.7%
p.K666E	14	2	0.7%
p.Y623C	14	1	0.4%
p.R625H	14	1	0.4%
p.H662D	14	1	0.4%
p.V701F	15	1	0.4%
p.K741N	15	1	0.4%
p.D894G	18	1	0.4%

**Supplementary Table 12.** Genes predicted to be alternatively spliced in *SF3B1* mutated and unmutated cases

Gene Symbol	Cluster ID	RefSeq	p-value
DENND2C	2429147	NM_198459	3.00E-23
WWC1	2839543	NM_001161661	1.37E-18
SEL1L3	2764192	NM_015187	2.78E-16
CRNKL1	3899954	NM_016652	5.91E-15
SEC14L1	3735752	NM_001143998	1.90E-14
ZKSCAN5	3014855	NM_014569	2.56E-14
ADAR	2436754	NM_001111	1.26E-13
CASC3	3720739	NM_007359	2.54E-12
TP53BP1	3621194	NM_001141980	8.18E-12
C10orf46	3309124	NM_153810	3.63E-11
OTUD5	4007643	NM_017602	6.56E-11
LRRFIP2	2669184	NM_006309	6.87E-11
C10orf137	3269587	NM_015608	9.76E-11
OSBP	3374698	NM_002556	9.85E-11
BCL9	2356818	NM_004326	1.01E-10
ZNF274	3843797	NM_133502	1.67E-10
SH2B3	3431892	NM_005475	1.97E-10
ATP11C	4024160	NM_173694	1.99E-10
TGIF1	3776504	NM_170695	2.24E-10
FAM82A2	3619595	NM_018145	2.39E-10
GLS	2520291	NM_014905	2.48E-10
MTMR10	3615985	NM_017762	2.80E-10
TRIM33	2429069	NM_015906	2.84E-10
CGRRF1	3536396	NM_006568	3.30E-10
CEP76	3799542	NM_024899	3.81E-10
ELAC2	3746040	NM_018127	5.16E-10
CCAR1	3249788	NM_018237	5.43E-10
TM9SF4	3881686	NM_014742	1.02E-09
PTDSS1	3108072	NM_014754	1.03E-09
ZMYM6	2405992	NM_007167	1.23E-09
WHSC1L1	3131916	NM_023034	2.39E-09
TFE3	4007734	NM_006521	3.39E-09
MTMR1	3994846	NM_003828	3.94E-09
PTPN1	3888721	NM_002827	3.95E-09
NCOA3	3887635	NM_181659	4.15E-09
MAP3K5	2975867	NM_005923	4.71E-09
RNF149	2567583	NM_173647	5.48E-09
EPC1	3284073	NM_025209	5.89E-09
NDUFA10	2606574	NM_004544	8.25E-09
DCAF13	3110341	NM_015420	1.20E-08
C3orf25	2694753	BC066975	1.57E-08
RNF216	3036985	NM_207111	1.60E-08
FBXL20	3755655	NM_032875	1.95E-08
PLK4	2742985	NM_014264	2.31E-08

ASNSD1	2519860	NM_019048	2.66E-08
AKAP8	3853299	NM_005858	3.20E-08
LMBR1L	3453774	NM_018113	3.63E-08
C8orf41	3130823	NM_025115	4.21E-08
ABCF3	2655511	NM_018358	4.93E-08
MIR650	3938384	NR_030755	5.10E-08
TAP2	2950167	NM_000544	5.27E-08
HARS	2878474	NM_002109	5.90E-08
C11orf30	3340913	NM_020193	6.05E-08
DDX3X	3974838	NM_001356	6.28E-08
NAPB	3901191	NM_022080	7.62E-08
DLAT	3348852	NM_001931	7.93E-08
SNAP29	3937755	NM_004782	8.07E-08
TNRC6A	3653398	NM_014494	9.00E-08
EIF3B	2987441	NM_001037283	1.16E-07
IARS	3214668	NM_013417	1.24E-07
CDK5RAP1	3902983	NM_016408	1.26E-07
ARID1B	2932928	NM_017519	1.38E-07
CAST	2821194	NM_001750	2.01E-07
PEX1	3061191	NM_000466	2.20E-07
SFMBT1	2676518	NM_001005159	2.30E-07
ZNF585A	3860737	NM_152655	2.79E-07
TBCK	2780734	NM_001163436	2.82E-07
COPS5	3138978	NM_006837	3.10E-07
KIF6	2952959	NM_145027	4.09E-07
ZC3H14	3547610	NM_024824	4.10E-07
PGRMC2	2785114	NM_006320	4.81E-07
GABRA3	4026075	NM_000808	4.91E-07
TOPBP1	2695941	NM_007027	4.93E-07
EDEM2	3903778	NR_026728	5.99E-07
LATS2	3504526	NM_014572	6.05E-07
USP36	3772581	NM_025090	6.54E-07
MARCH10	3766013	NM_152598	7.08E-07
DNAJC17	3619650	NM_018163	7.29E-07
SMC5	3174224	NM_015110	8.29E-07
UCK1	3227645	NM_031432	8.53E-07
ZER1	3226661	NM_006336	9.19E-07
PPIL2	3938244	NM_014337	9.70E-07
MTMR3	3942179	NM_021090	1.09E-06
BCL10	2420808	NM_003921	1.11E-06
NRF1	3023565	NM_005011	1.16E-06
CPSF2	3548788	NM_017437	1.29E-06
FAF1	2412082	NM_007051	1.30E-06
USP33	2419113	NM_015017	1.31E-06
RBBP6	3653317	NM_006910	1.38E-06
STRADA	3766284	NM_153335	1.40E-06
UBOX5	3895232	NM_014948	1.46E-06
DDHD1	3564997	NM_001160148	1.59E-06
ZC3HAV1	3075566	NM_020119	1.64E-06
UBE2D3	2779992	NM_181892	1.90E-06

SNCA	2777714	NM_000345	2.35E-06
ORC2L	2594569	NM_006190	2.35E-06
FANCD2	2610241	NM_033084	2.37E-06
RNF25	2599536	NM_022453	2.56E-06
FBXW11	2886977	NM_033644	2.58E-06
MCM9	2971692	NM_153255	3.25E-06
ZFP91	3331730	NM_053023	3.37E-06
STAMPB	2488959	NM_213622	3.47E-06
TRIM8	3261820	NM_030912	3.86E-06
HIP1R	3435548	NM_003959	3.94E-06
NAP1L4	3359469	NM_005969	3.97E-06
PAF1	3861978	NM_019088	4.24E-06
NFKB1	2737717	NM_003998	4.27E-06
EBP	3976670	NM_006579	4.73E-06
TERF2	3696571	NM_005652	4.99E-06
BUB3	3268669	NM_004725	5.44E-06
HTATSF1	3992521	NM_001163280	5.53E-06
TMEM154	2790062	NM_152680	5.76E-06
CDK16	3976124	NM_006201	6.07E-06
RASGRF1	3634852	NM_002891	6.26E-06
ERP44	3217736	NM_015051	6.61E-06
VHL	2610336	NM_000551	6.97E-06
TMCC1	2694931	NM_001017395	7.03E-06
RAD50	2828564	NM_005732	7.12E-06
IFRD2	2675088	NM_006764	8.74E-06
POTEA	3096638	NM_001005365	9.09E-06
PLCH2	2316605	NM_014638	9.50E-06
ELF5	3369117	NM_198381	9.67E-06
HNRNPM	3819543	NM_005968	1.00E-05
ACOT2	3543673	NM_006821	1.01E-05
CTSS	2434575	NM_004079	1.09E-05
OSGIN2	3106276	NM_004337	1.12E-05
TWSG1	3778372	NM_020648	1.33E-05
HOOK3	3096368	NM_032410	1.39E-05
WDR55	2831619	NM_017706	1.39E-05
TMX1	3535395	NM_030755	1.64E-05
OGFOD1	3662041	NM_018233	1.71E-05
MGEA5	3304012	NM_012215	1.81E-05
BTN2A1	2899437	NM_078476	1.90E-05
SENP6	2913983	NM_015571	1.95E-05
SRRD	3941010	NM_001013694	2.09E-05
DUSP12	2363902	NM_007240	2.19E-05
JTB	2436401	NM_006694	2.24E-05
ZNF562	3849549	NM_001130031	2.28E-05
MICALL1	3945084	NM_033386	2.45E-05
ICK	2957499	NM_016513	2.71E-05
GTDC1	2579439	NM_001006636	2.79E-05
FAS	3257098	NM_000043	2.92E-05
ARL8A	2451139	NM_138795	3.26E-05
STXBP5	2929870	NM_001127715	3.42E-05

EIF2C3	2330133	NM_024852	3.72E-05
CYP2E1	3272981	NM_000773	4.09E-05
SRP68	3771297	NM_014230	4.37E-05
HCP5	2902326	NM_006674	4.77E-05
DDX46	2829488	NM_014829	5.07E-05
IMPDH2	2673873	NM_000884	5.46E-05
SP140	2531233	NM_007237	5.54E-05
SART3	3470253	NM_014706	5.72E-05
SLC30A5	2813364	NM_022902	6.21E-05
CXCL5	2773369	NM_002994	6.68E-05
MAP2K4	3710681	NM_003010	6.80E-05
ZDHHC3	2671652	NM_016598	6.89E-05
CD47	2687739	NM_001777	6.97E-05
C7orf10	2998638	NM_024728	7.77E-05
TOX2	3886294	NM_032883	8.54E-05
DEK	2944068	NM_003472	8.85E-05
FAM32A	3823613	AF151902	8.95E-05
PIGS	3750740	NM_033198	9.37E-05
PSIP1	3199790	NM_033222	0.0001
ZNHIT1	3016211	NM_006349	0.00011
FAM190B	3255402	NM_018999	0.00012
CUZD1	3310675	NM_022034	0.00013
CAMK2A	2881300	NM_015981	0.00013
MYH6	3557430	NM_002471	0.00013
NSFL1C	3894637	NM_016143	0.00014
SFRS5	3542207	NM_001039465	0.00014
STAG3	3015338	NM_012447	0.00016
RNF146	2924898	NM_030963	0.00018
SRP19	2824286	NM_003135	0.0002
BMP2K	2732942	NM_198892	0.0002
KIAA1586	2911257	NM_020931	0.00021
GTF3C3	2593352	NM_012086	0.00021
TRIM22	3318443	NM_006074	0.00022
SLC7A14	2705030	NM_020949	0.00022
CLDND1	2685908	NM_001040199	0.00023
CDHR3	3018011	NM_152750	0.00029
GCC1	3071285	NM_024523	0.00029
BBS4	3600960	NM_033028	0.00031
KIAA1009	2962998	NM_014895	0.00033
SMAD5	2830010	NM_001001419	0.00033

**Supplementary Table 13.** Validated splicing targets affected by *SF3B1* mutation in CLL patients

Gene	Junction	Junction coverage (RPKM $\pm$ s.e.m.)		Gene coverage (RPKM $\pm$ s.e.m.)	
		<i>SF3B1</i> <sup>MUT</sup>	<i>SF3B1</i> <sup>WT</sup>	<i>SF3B1</i> <sup>MUT</sup>	<i>SF3B1</i> <sup>WT</sup>
<i>FOXP1</i>	chr3: 71,019,346-71,019,887	324 $\pm$ 44	27 $\pm$ 19	17 $\pm$ 2	17 $\pm$ 2
<i>SLC23A2</i>	chr20: 4,843,573-4,848,416	65 $\pm$ 9	0 $\pm$ 0	32 $\pm$ 5	29 $\pm$ 2
<i>TCIRG1</i>	chr11: 67,815,440-67,815,554	236 $\pm$ 38	7 $\pm$ 6	110 $\pm$ 57	76 $\pm$ 15

**Supplementary Table 14.** Clinical and biological features of the 279 CLL patients included in the validation study

Parameter	Category	<i>SF3B1</i>	<i>SF3B1</i> mutated	p
		unmutated (n=252)	(n=27)	
Gender	Male (%)	144 (57%)	19 (70%)	ns
Age (years), median (range)		58 (24-93)	54 (33-82)	ns
Binet stage*	A	206 (82%)	16 (59%)	0.004
	B	38 (15%)	11 (39%)	
	C	6 (2%)	0 (0%)	
Rai stage*	0	146 (58%)	7 (26%)	0.004
	I-II	95 (38%)	19 (70%)	
	III-IV	9 (4%)	1 (4%)	
Lymphocytes (x10 <sup>9</sup> /L), median (range)	13.2 (1.7-337)	19.0 (3.2-111)	ns	
Hemoglobin (g/L), median (range)	139 (63-175)	140 (108-165)	ns	
Platelets (x10 <sup>9</sup> /L), median (range)	200 (19-470)	180 (106-456)	ns	
LDH	>UNL	21/226 (9%)	3/25 (12%)	ns
β <sub>2</sub> -microglobulin	>UNL	50/204 (25%)	13/25 (52%)	0.008
Lymphocyte doubling time	< 1 year	31/153 (20%)	5/15 (33%)	ns
CD38	High	58/218 (27%)	10/21 (48%)	ns
ZAP-70	High	60/207 (29%)	12/24 (50%)	ns
IGHV	Unmutated	58/128 (45%)	15/21 (79%)	0.03
<i>NOTCH1</i>	Mutated	20/244 (8%)	5/16 (31%)	0.01
5-year time TTP (95% CI)	Binet stage A	34% (27-42)	73% (51-96)	0.002
10-year time to Richter (95% CI)	All	10% (8-12)	9% (0-21)	ns
10-year OS (95% CI)	All	77% (70-84)	30% (6-54)	0.002
Follow-up (years), median (range)	6.4 (0.1-25)	4.1 (0.5-11.9)	ns	

CD38 high: ≥30% positive CLL cells; ZAP-70 high: ≥ 20% positive CLL cells; *IGHV* unmutated: ≥ 98% homology with germline; TTP: time to progression; OS: overall survival. \*Stage information was not available for two patients.



**Supplementary Table 15.** Main clinical and biological features with prognostic relevance in 279 patients with CLL

Parameter	Category	N	5-year OS	10-year OS	P value
All patients	All	279	89.8	70.4	-
Binet stage	A	218	91.6	76.4	0.004
	B	48	85.3	55.3	
	C	6	66.7	44.1	
Rai stage	0	150	92.1	82.3	<0.001
	I-II	112	89.9	61.1	
	III-IV	10	52.5	35	
ZAP-70	Low	158	95.4	85.2	0.002
	High	72	87.3	59.2	
CD38	Low	169	93.6	80.5	0.004
	High	67	87.3	57.8	
<i>IGHV</i>	Unmutated	72	90.7	48.5	0.003
	Mutated	77	92.3	90.1	
<i>NOTCH1</i>	Unmutated	235	90.5	72.3	0.05
	Mutated	25	72.2	36.1	
<i>SF3B1</i>	Unmutated	252	90.3	76.8	0.002
	Mutated	27	84.9	29.8	

**Supplementary Table 16.** Primers used for quantitative polymerase chain reaction

Gene	Form	Sequence
TCIRG	Truncated	5'-CCAACGTCACCGGTGTCTTC-3'
		5'- TCTGCCTCTTGCTGAGGAA-3'
	Control	5'- CCAGGATGACGGACATCTTCA-3'
		5'- CCAACGTCACCGGTGTCTTC-3'
SLC23A2	Truncated	5'-TTCATCCAGTCCCAACATTGG-3'
		5'-CTGCCGACCTGCAGAACAC-3'
	Control	5'- TTCATCCAGTCCCAACATTGG-3'
		5'-CATGCCAGAGCGAGCAT-3'
FOXP1	Truncated	5'- CCTACTGCACACCTCTCAATGC-3'
		5'-CTGGTACCATTGGTGATGTAACAAG-3'
	Control	5'- CCTACTGCACACCTCTCAATGC-3'
		5'-CATGGAAGCGGTAGTGTATAGAGGT-3'